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THE NEWER ASPECTS OF OLFACTORY PHYSIOLOGY AND THEIR DIAGNOSTIC APPLICATIONS

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During ordinary breathing and during sniffing of odors air currents are the chief factors concerned in the transportation of odorous particles to the olfactory membranes. The larger part of the inspired air and odor passes backward into the nasopharynx, and only a small part, deviated from this course, is directed to the superior meatuses and there affects the specific olfactory receptor cells. These receptor cells initiate the impulse which is transmitted to the olfactory centers in the brain.

The perception and identification of odors are conditional on stimulation of the receptor cells, which in turn depends on several factors: (1) a sufficient mass of odorous particles must come into contact with the olfactory receptors; (2) in order to produce an adequate stimulus, the stream of air carrying the odor must impinge on the olfactory membrane with a certain degree of force, and (3) the identification of many odors depends not only on sufficient volume and force but on the effect on the sensory receptors of the trigeminal nerve. Until the procedures had been devised by which a measured volume of air containing odorous particles was injected into the nasal passages under a known pressure, it was not possible satisfactorily to measure the volume that reached the olfactory receptors during breathing and the force with which the stream of air carrying the odor impinged against the olfactory membrane or to determine the effects of many odors on the trigeminal nerve. In a series of experiments my colleagues and I found that if air carrying an odor is injected into the nasal passages in sufficient volume and with sufficient force, the odor can be recognized even when the breath is being held; in papers recently published two procedures for the examination of the sense of smell were described, which are based on this new principle. These procedures were called "blast injection" and "stream injection."

By the procedure of blast injection the factor of nasal inhalation is excluded and a measured volume of air containing odorous particles is released into one or both nasal passages under a known pressure. The

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injection is given in the optimum direction, directly toward the olfactory membrane. By this means the factor of uncertainty regarding the volume of air containing odorous particles that enters the nasal passages is avoided, and the known pressure under which the blast of air carrying the odor is injected takes the place of the force of the inspiratory movement of breathing. It was therefore possible to establish exact numerical values for different odors. The smallest number of cubic centimeters of air carrying an odor that can be identified was called the minimum identifiable odor (M.I.O.) of the odorous substance.

In the procedure of blast injection the volume of the injected air and its pressure are known. It was therefore possible to investigate the relative importance of volume and pressure of the olfactory stimulus and to conclude that for the perception and identification of an odor the force with which the odorous particles impinge on the olfactory cells in the superior meatus of the nose is of more importance than the volume that is injected.

In a second procedure, which was called stream injection, the air containing odorous particles is injected into one or both nasal passages in a continuous stream for various periods and at varying volume rates, while the subject is breathing through the mouth.

The procedure of stream injection was found to be of value both for the study of olfactory fatigue and for investigation of the effects of odorous substances on the trigeminal nerve. The odorous substances of which the effects were purely olfactory could be distinguished from those that affected the trigeminal nerve also, and it was found that many substances hitherto believed to be purely olfactory stimulants have an effect on both the olfactory and the trigeminal nerve.

By means of the stream injection of air carrying the odors it was possible to produce olfactory fatigue of different duration, and then by means of blast injection, to determine the relation between the duration and volume rate of the stream injection and the depth and duration of the resulting fatigue and to gain some insight into the nature of olfactory fatigue and the parts of the brain responsible for this alteration of function. The fatigue produced by the stream injection of air carrying an odor was mainly specific for the substance used, but fatigue for one odor also caused some diminution of the acuity of smell for other odors.

By the use of blast and stream injections I was able to study the effect of unilateral olfactory stimulation on birhinal acuity of smell, and the effect of bilateral stimulation on monorhinal acuity of smell.

THE NORMAL PHYSIOLOGY OF OLFACTION AND THE NATURE OF THE OLFACTORY PROCESS

The blast injection tests demonstrate that the efficiency of the olfactory receptors is almost the same in all healthy persons and that normal

differences in acuity of smell during breathing or sniffing of odors are due mainly to variations in the form and shape of the nasal passages.

If the size and shape of the two nasal passages are the same and an odor is inhaled birhinally, the odor reaches the olfactory membranes of the two sides at the same moment (bisynchronorhinal smell). If, however, there is an abnormality in the form of the nasal passages (such as hypertrophy of the turbinate bone, spurs or perforation of the septum), so that during breathing the stream of air carrying the odor is not properly directed to the olfactory membranes, an insufficient volume reaches the olfactory cells or the force with which the inhaled stream of air carrying the odor impinges on the receptor cells is too low. As a result, the olfactory stimulus is relatively weak and the sense of smell of the subject is relatively poor.

If one nasal passage is completely obstructed, the inhaled odor can reach the olfactory membrane of only one nasal passage, and unless this is compensated for the ability of the person to perceive and to identify odors is less than the average. If one nasal passage is partially obstructed, the entry of odor into the superior meatus is less on that side than on the other. On the affected side there may also be a delay before the odor reaches the olfactory membrane, so that birhinal smell is not bisynchronorhinal, and the sense of smell of the person may be less acute than that of others.

The effect of the olfactory stimulus on the specific receptor cells in the superior meatus is greatly influenced by a number of factors. Some of these are extraneous and are dependent on variations in the size and shape of the nasal passages to which reference has just been made. The olfactory stimulus may be inadequate because of alterations in the olfactory cells due to acute or chronic inflammatory disease of the lining membrane of the nasal passages. In acute rhinitis, the olfactory cells may be temporarily deprived of function or the olfactory membrane in the superior meatus is covered by secretions, so that the odor cannot reach the olfactory cells or reaches them imperfectly. Temporary olfactory hyperacuity may occur just before and during the menstrual period.

The Olfactory Impulse.—Studies made by the blast injection and stream injection of air carrying odors yielded considerable information regarding the laws which govern the transmission of the olfactory impulse from the receptor cells of the olfactory membrane to the cerebral centers for the perception and identification of odors. An extended series of tests on healthy persons and on persons with intracranial tumor demonstrated that the olfactory impulse is governed by laws which are similar to if not the same as those which nerve impulses through somatic neural pathways obey. If the transmission of impulses through the extracerebral olfactory pathways (olfactory nerve, bulb, tract, external or internal olfactory root) is interfered with by direct pressure, the M.I.O. (that is, the smallest volume of air carrying an odor which can

be identified when injected into one or both nasal passages) is elevated above the normal figure. In other words, when there is a mechanical block of any part of the extracerebral olfactory structures, the stimulus must be stronger if it is to be effective. However, just as in somatic nerves, after the impulse has traversed the region of the partial block it is transmitted to the centers in the brain with normal intensity.

The investigations of olfactory fatigue by the stream injection of air carrying odors in patients with tumor in one cerebral hemisphere demonstrated that, as suspected many years ago by Luciani, the connections between each olfactory membrane and the olfactory centers in the brain are predominantly, although not entirely, homolateral. The nerve impulse initiated by an adequate stimulation of the cells of one olfactory membrane is transmitted mainly to the primary and secondary olfactory centers of the same side of the brain. In birhinal smell, however, there is a summation of impulses from the two olfactory membranes, and this summation is of great physiologic significance.

We compared the values for the M. I. O. determined by monorhinal blast injection tests of normal persons with the values obtained when the injection was birhinal. When air carrying an odor is injected unilaterally it all passes into one nasal passage through one branch of the nosepiece. When double the volume used in the first test is injected through a bilateral nosepiece, the volume that is released into each nasal passage is the same as that which enters one nasal passage in a unilateral blast injection. For example, on monorhinal injection, the M. I. O. for citral is between 6 and 8 cc.; if there was no summation of impulses from the two olfactory membranes the M. I. O. on birhinal injection should be between 2 times 6 and 2 times 8, or between 12 and 16 cc. By actual tests the value is shown to be between 9 and 11 cc., and from this fact one might be led to conclude that in birhinal smell there is a summation of impulses from the two olfactory membranes. This conclusion is not justified for the following reasons: When 11 cc. of air is injected into the test bottle of citral and is released as blasts into the two nasal passages, 5.5 cc. enters each side, but the pressure is not the same as the pressure of 8 cc. injected into the bottle and released into one nasal passage. In the first instance the volume of the blast into each nasal passage is smaller, but the pressure of each blast is higher than that used for the injection into one nasal passage.

In order to determine the value of the M. I. O. on birhinal injection when the blast released into each nasal passage is under the same pressure as or under a lower pressure than the blast of a unilateral injection, a different procedure was used. The apparatus devised for the purpose has been described in detail in a recently published paper.[1]

1. Elsberg, C. A.: The Sense of Smell: XIII. The Summation of Olfactory Impulses from the Two Olfactory Membranes and Its Physiological Significance, Bull. Neurol. Inst. New York **4**:544, 1936.

By this procedure it was possible to demonstrate that when an odor is given birhinally, the minimum volume and pressure of the blast into each nasal passage which are necessary for identification of the odor are less than the volume and pressure necessary for the M. I. O. on unilateral injection. This was absolute proof that there is a summation of the impulses from the two olfactory membranes.

In the experiments referred to the blasts of air carrying the odor were released into the two nasal passages at the same time; therefore, the stimulation of the olfactory receptors of the two sides was simultaneous. Summation of impulses still occurred when there was an interval between the releasing of the blast into the two nasal passages. The time that could be permitted to elapse between the blasts without loss of the ability to identify the odor was shorter as the volume of the blast was diminished.

Therefore, there is a definite period during which the olfactory impulse affects the cerebral olfactory centers, and summation will still occur during this period. The more powerful the stimulus (and therefore the impulse) the longer will be the time during which the cells in the brain are affected.

The results of these studies showed that for the identification of odors there is an advantage when the odor is inhaled birhinally. When the olfactory receptors of the two nasal passages are simultaneously stimulated, the effect of the olfactory impulse from one side is superimposed on that of the other. Under these conditions a smaller volume introduced into each nasal passage can be identified than the sum of the volume necessary for identification of the odor when the blasts are introduced separately into the two sides of the nose. To a considerable extent summation appears to depend not only on the odor that affects the specific receptors of the second nasal passage but on the stimulus produced and the impulse initiated by an increase of pressure on that olfactory membrane. Summation will occur (although not to the same degree) when fresh air under pressure is injected into one nasal passage and air carrying an odor is injected into the other. This fact was additional evidence of the importance of pressure for the effectiveness of the olfactory stimulus.

The effect of the olfactory stimulus on the specific receptor cells in the brain depends on the strength of the olfactory impulse. The impulse is used up by the receiving cells, and therefore the duration of the effect on the central cells is conditioned on the strength of the impulse, and the rapidity with which the impulse is used up depends on the activity of the specific receiving cells. When the impulse is of adequate strength to interfere temporarily with function altogether, there is olfactory fatigue. The duration of the fatigue depends on the strength and

the duration of the stimulus (and impulse) and the condition of the cells themselves.

This reciprocal relation between the efficiency of the receptor cells of the olfactory centers and the strength of the impulses which reach them is well illustrated by the results of olfactory tests with coffee and citral and by the homolateral increased duration of fatigue in persons with tumor of the brain.

Tests with coffee and citral by the method of blast injection had demonstrated that as an olfactory stimulant citral is more powerful than coffee, so that the M. I. O. is smaller and the duration of fatigue produced by steam injection of air carrying the odor more prolonged with the former than with the latter substance. This relation is illustrated in the diagram shown in figure 1, in which *A* represents the mass of receiving cells in the brain and *b* the strength of the olfactory

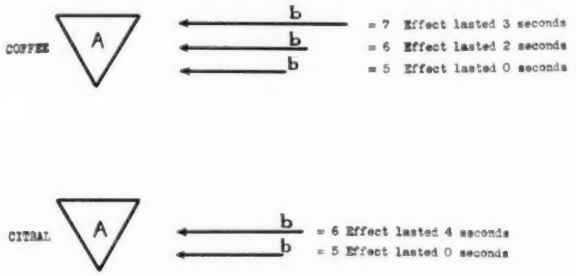

Fig. 1.—The reciprocal relation between impulse and specific receptor cells in the brain when summation tests with the odors of coffee and citral were made. The numbers *7*, *6* and *5* signify the number of cubic centimeters of air injected into each bottle. The explanation of the time periods is given in the text. The statement that for *5* the effect lasted 0 seconds means that the effect lasted for less than one second.

stimulus. Tests of summation showed that when *b* is relatively strong, its effect is prolonged. When in the case of the odor of coffee *b* was 7, the effect of the impulse lasted for three seconds because summation would still occur with a three second interval between the blast injections into the two nasal passages; when *b* was 6, the effect lasted for two seconds; when *b* was 5, summation occurred only on bilateral synchronous blast injections of the air carrying the odor. With citral, on the other hand, the effect of the impulse lasted longer. When, for example, *b* was 6, the effect lasted for four seconds. This showed that the olfactory effect of the odor of citral is greater than that of the odor of coffee and made it clear why in the normal person olfactory fatigue produced by the odor of citral lasts longer than that produced by the odor of coffee.

A similar diagram shown in figure 2 serves to explain the prolongation of unilateral fatigue which occurs in patients with a tumor within the substance of one cerebral hemisphere. In a patient with a glioma in the right cerebral hemisphere the duration of fatigue produced by a stream injection of air containing the odor of coffee for thirty seconds was one and five-tenths minutes on the left and six and five-tenths minutes on the right side. In other words, there was marked prolongation of olfactory fatigue on the same side as that of the subcortical neoplasm. This indicated either that the functioning cells in the olfactory centers were less efficient or that the active cells were fewer. In figure 2, A' is drawn smaller than A to indicate this. The effect of identical stimuli (which give rise to impulses of equal strength) is prolonged in A' because, either on account of a smaller number of functioning cells or because of decreased efficiency of all the cells or both, the olfactory impulse is used up more slowly and the result on the cells is of longer duration.

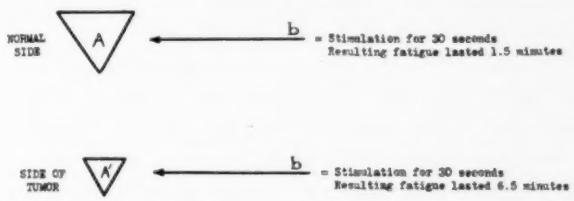

Fig. 2.—The reciprocal relation between the impulse and its effect on the specific receptor cells of the two sides of the brain of a patient with subcortical glioma in one cerebral hemisphere. The stimulus (and the primary impulse) were the same on the two sides, but the fatigue was prolonged on the side of the tumor. In the hemisphere in which the tumor lay the relation between intensity of impulse and mass or efficiency of receptor cells was different from that of the normal side.

Because so little is known of the process by which the particles or molecules of an odorous substance stimulate the olfactory receptors, the results of investigations of the physiology of the sense of smell have been difficult of interpretation. Most writers believe that the odorous particles become dissolved in the thin layer of lipoid fluid which coats the olfactory epithelium and bathes the fine nerve filaments which end almost on the surface of the olfactory cells. Even if this view were correct, part of the process would be physical and would be dependent on the well known relation between the pressure and the solubility of a gas or vapor in a liquid. The investigations of Henry demonstrated that the amount of gas or vapor dissolved by a liquid is proportional to the pressure to which the gas or vapor is subjected. Therefore, even if the olfactory cells are chemoreceptors, the pressure with which a stream of air carrying the odor impinges on the liquid coating of the

olfactory cells must be of significance for the amount of odorous substance that is dissolved in the lipoid fluid. It is reasonable to believe that the olfactory stimulus is based on the combined effects of molecular activities, which are called wavelengths, and of the force with which the odorous particles or molecules impinge on the lipoid fluid which coats the olfactory cells. If the change is entirely physical, olfaction is a physical process, the combined effects of molecular activity and of pressure are transmitted to the terminal filaments of the olfactory nerve as the stimulus which starts the olfactory impulse and the olfactory cells are mechanicoreceptors. On the other hand, if the physical changes are significant only for the degree of penetration of the odor into the lipoid fluid, the olfactory cells may be chemoreceptors. Even if the latter hypothesis is correct, olfaction is basically a physical process.

THE LOCALIZATION OF OLFACTORY FUNCTION IN THE BRAIN

Our studies of olfaction in healthy persons and in those with intracranial lesions have made it possible to draw some conclusions regarding the cerebral localization of olfactory functions.

That the pathways from each olfactory membrane to the brain are predominantly homolateral has already been mentioned. The results of investigations of olfactory fatigue in healthy persons demonstrated that impulses from the receptor cells of each nasal passage reach both sides of the brain. Furthermore, acuity of smell of one side of the nose can be influenced by added stimulation of the olfactory receptors of the other side. Therefore, olfactory impulses must cross in either the anterior or the hippocampal commissure. For reasons given in another report, it is highly probable that a number of olfactory fibers cross to the other side in the anterior commissure, so that *sensu stricto* this structure is a chiasm.

There is some evidence to support the belief that the hippocampal commissure is concerned in the summation of impulses that occurs in birhinal smell. Studies made of patients with a tumor underneath one or both frontal lobes (particularly in large growths involving the pituitary gland) which was of such size and in such a situation that the anterior commissure must have been pressed on showed that summation from the two olfactory membranes was as good as that in normal persons. Therefore, there must be some pathway for summation other than the crossing fibers of the anterior commissure. In two patients with deep tumor in the temporal lobe, which extended to or across the midline, there was absolutely no evidence of summation of olfactory impulses. The absence of any interference with summation when the anterior commissure is compressed and the absolute loss of summation in the last cases referred to suggest that the hippocampal commissure

(or possibly the corpus callosum itself) is concerned in the summation of impulses in birhinal smell.

The investigations of the duration of olfactory fatigue in expanding lesions in certain parts of the cerebral hemipheres have led me to the conclusion that the structures concerned in fatigue of the sense of smell are in the brain itself and in the parts of the brain that have to do with the perception and the identification of olfactory impressions. Furthermore, recent studies seem to make it probable that olfactory fatigue is due to a temporary block in the pathways from the cells that have to do with perception to those that have to do with the identification of odors.

From the results of olfactory tests of patients with tumor of the corpus callosum, particularly in one instance in which a very small and circumscribed growth produced marked alterations of olfactory fatigue, we have been led to suspect that the corpus callosum may have an important function in olfaction and that it must be included in the olfactory sphere.

In two patients who suffered from olfactory hallucination due to a small tumor in the anterior part of one uncus, the olfactory tests showed an elevation of the M. I. O. on the affected side. This physiologic evidence may be taken to confirm the histologic observation that the fibers of the external olfactory root are mainly destined for the uncus.

THE CLINICAL SIGNIFICANCE OF STUDIES OF OLFACTION BY THE BLAST INJECTION AND STREAM INJECTION OF ODORS

"Human receptors belong to one or other of two classes. Either they are concerned purely and simply with the excitation of reflex acts and take no part in the production of sensations, . . . or they are at the same time effective in arousing sensations, the elements of intellectual life, and hence may be appropriately called sense organs" (Parker). Much attention has been devoted to the eye and the ear and little to the organs of smell and taste. The results of studies of the olfactory sense briefly outlined in this paper indicate that smell in man, though not as necessary for nutrition as in the lower vertebrates, must still be considered an important function, significant of high mental activity, governed by laws similar to, if not identical with, those which the other special senses and indeed all somatic sensibility obey, and often profoundly disturbed in diseases that affect the pathways and centers which have an olfactory function.

It was natural, therefore, that after the physiology of normal olfaction had been studied by the new quantitative olfactory tests the alterations that occurred in intracranial disease should be investigated. If there were characteristic changes from what might be called the normal olfactory pattern in lesions in different parts of the olfactory pathways, this altered pattern might indicate the location of the intra-

cranial disease. The tests may therefore be of value for the localization of tumor of the brain. A summary of our results in more than 150 cases of intracranial tumor is given in the following paragraphs.

1. When a neoplasm exerts pressure on one olfactory nerve, the M. I. O. of that side is higher than normal and a larger quantity of air carrying the odor has to be injected into that side of the nose before the odor can be identified. If both olfactory nerves, bulbs or tracts are involved, the M. I. O. is higher on both sides, the greatest elevation being found on the side that is most affected. If the duration of olfactory fatigue is not longer than normal while there is this unilateral or bilateral diminution of olfactory acuity, the neoplasm is situated on the under-surface of one or both frontal lobes and is outside the brain tissue. This alteration of olfactory pattern was found in 25 of 26 instances of verified subfrontal tumor, in which were included cases of suprasellar and parasellar meningioma, aneurysm of the internal carotid artery or the anterior part of the circle of Willis and tumor of the pituitary gland. In a person with a pituitary adenoma that has not extended upward beyond the confines of the sella turcica the olfactory pattern is normal, but if the growth projects above the sella turcica the olfactory tracts are subjected to pressure and the M. I. O. of one or both sides is elevated. In brief, the unilateral olfactory tests by means of the blast injection and stream injection of air carrying odors have demonstrated that in pressure on the olfactory nerve, bulb, tract, external olfactory (and probably mesial olfactory) root, the M. I. O. of the same side is elevated, while the duration of olfactory fatigue caused by a stream injection for thirty seconds of air carrying the odor is not prolonged beyond the normal. This combination of elevation of the M. I. O. and normal duration of fatigue is encountered in persons with a tumor in the anterior cranial fossa underneath one or both frontal lobes of the brain.

2. In instances in which intracerebral tumor or a large dural growth has become buried in the brain the M. I. O. is not raised but the duration of fatigue is prolonged on the side on which the neoplasm is located. This alteration is especially marked when the growth is situated in the frontal, temporal or parietal lobe and is subcortical, but it may not be found in the slow-growing meningiomas in the occipital lobes.

3. The combination of unilateral elevation of M. I. O. and prolonged duration of fatigue on the same side is characteristic of tumor within the substance of one frontal lobe which directly or indirectly exerts pressure on one olfactory nerve, bulb or tract. This alteration of olfactory pattern was found in 21 patients with a verified tumor in the substance of one or the other frontal lobe on whom olfactory tests were made.

4. When there is a tumor in or near the midline of the cranial cavity, such as an infiltrating growth which extends to the mesial surface of one cerebral hemisphere or a tumor which involves the corpus callosum, the duration of fatigue produced by the stream injection of air carrying an odor is prolonged and lasts for more than ten minutes. In patients with a primary tumor of the corpus callosum or of a growth which secondarily involves this structure the duration of fatigue may be prolonged on both sides.

5. Patients with a generalized increase of intracranial pressure often show an increased irritability of the olfactory pathway, so that the M. I. O. is lower than normal. This smaller M. I. O. is often found in other intracranial diseases, but unless it is associated with characteristic alterations in the duration of olfactory fatigue it does not have any significance for localization.

As the elevation of the M. I. O. and the prolongation of fatigue are so significant for the localization of a tumor of the brain, it is important to appreciate that alterations from the normal olfactory pattern may occur in a variety of diseases other than tumor. If there is a pathologic change in any part of the extracerebral olfactory pathways as a part of an inflammatory or vascular disease of the brain, the M. I. O. may be elevated.

Diminution or loss of smell is frequent after severe cranial trauma, and in a number of patients with this condition the M. I. O. is larger than normal. This is to be explained as the result of avulsion of filaments of the olfactory nerve out of the foramina in the cribriform plate of the ethmoid sinus.

In three cases of turricephaly in which we had occasion to test the acuity of smell, it was greatly diminished. In this abnormality of cranial structure the olfactory nerves, bulbs and tracts must have been distorted or have been pulled on for a long period, with resulting changes in these structures which produced an elevation of M. I. O. or complete anosmia.

In all the aforementioned conditions the elevation of the M. I. O. might make one think of an expanding lesion making direct pressure on the extracerebral olfactory pathways. Aside from the fact that in very few of the patients was tumor considered a possibility, the tests of the duration of olfactory fatigue usually showed deviations from the normal quite different from those observed in association with tumor of the brain.

The statements that have been made regarding elevation of the M. I. O. in diseases other than tumor of the brain are applicable also to prolongation of fatigue. Prolonged duration of fatigue is found in certain diffuse diseases of the central nervous system and in a variety of intracranial diseases. It has significance for the localization of tumor

of the brain only if it follows the definite pattern which has been described. I have examined a large number of patients with diffuse disease of the central nervous system and with localized intracranial lesions other than tumor. There are patterns of olfactory disturbance which appear to be characteristic of some other diseases. Thus, in many cases of encephalitis, especially if the parkinsonian syndrome is present, and in cases of paralysis agitans there is a remarkable fatigability of the olfactory sense. In persons with these conditions it is often difficult to obtain correct figures for the M. I. O. because of the great tendency to olfactory fatigue, and the duration of fatigue produced by the stream injection of air carrying the odor of citral or coffee is greatly prolonged on both sides.

In many patients who were suffering from the results of a cerebral vascular lesion the values for the M. I. O. and the duration of fatigue were within normal limits, but in a few there was prolongation of homolateral fatigue. These observations lead one to suspect that the increased duration of homolateral fatigue found almost regularly in persons with unilateral intracerebral tumor is due to some factor which exists in expanding lesions—perhaps a localized increase of pressure.

Up to the present time the new olfactory tests have been used only for the localization of tumors of the brain, and it has become possible to recognize olfactory patterns for intracranial growths in a number of situations. A larger experience may show that the tests have a limited value for differential diagnosis.

DISCUSSION

DR. ISRAEL STRAUSS, New York: I think the Association is to be congratulated that one of its members has found a method of quantitative estimation of a sensory function. I recall that scientists were obligated to Bárány, an otologist, for the discovery of a method by which the vestibular system can be studied and its function estimated quantitatively.

There are one or two questions I wish to ask Dr. Elsberg. First, has he studied cases of internal hydrocephalus in which there was no tumor? What are the results of such a condition on the olfactory system? Also, I wish to ask him how he can explain that in the case of a tumor involving the olfactory nerve or its roots, the minimal olfactory index is increased but the fatigability is not. How does he explain that a tumor in the frontal lobe, making no direct pressure on the olfactory nerve or the root, presents phenomena not only of increase in the minimal olfactory index but of increase in the duration of fatigue?

DR. TRACY J. PUTNAM, Boston: Dr. Elsberg has opened a great new field for the study of the central nervous system. It seems to me that it will be several years at least before the clinical significance of this series of tests is known exactly, but I am convinced from my own early attempts at the Boston City Hospital to follow in Dr. Elsberg's footsteps that it has an important place in neurologic examination. The technic must be carefully learned, and the rules which Dr. Elsberg has laid down must be followed with great care. There can be no question, however, that it introduces a quantitative element into a field which has been almost unexplored.

I should like to ask Dr. Elsberg in particular whether he has made further observations on any lesion but tumor and whether he has been able to lay down any criteria for the presence of tumor other than that in use for any local lesion in the production of abnormal physiologic behavior of the sense of smell. I think that the medical profession is witnessing the beginning of an important new branch of neurology.

DR. WILLIAM J. MIXTER, Boston: I believe that this is a very important addition to knowledge and diagnostic equipment. Dr. Elsberg is to be congratulated on the prospect of what is to be accomplished and gained by the application of his methods to the future study of patients.

DR. CHARLES A. ELSBERG, New York: In answer to the question of Dr. Strauss whether I have studied cases of hydrocephalus in which no tumor occurred, I wish to say that I have, but I have not thus far made summation studies in such cases. To my surprise I found that hydrocephalus in itself does not produce any alteration in what I call the olfactory pattern, i. e., it does not raise the value of the minimal olfactory index or of itself increase the duration of olfactory fatigue.

DR. ISRAEL STRAUSS, New York: Can you explain that observation, Dr. Elsberg, in view of the pressure on the olfactory tract?

DR. CHARLES A. ELSBERG, New York: As yet I am unable to explain it.

Dr. Strauss asked why in a subject with a tumor of the frontal lobe the minimal olfactory index is elevated but the duration of fatigue is not prolonged. The alteration that occurs is similar to that found by Lucas and Adrian in their well known experiments on nerve-muscle preparations. They, of course, were concerned with efferent impulses, while I was dealing with afferent impulses. If the nerve was blocked by pressure, a larger electrical stimulus was necessary, but when the impulse had passed the region of the block it proceeded on its course with normal intensity. A similar condition was found to obtain in patients with tumor which made direct pressure on the extracerebral olfactory pathways. If there was direct pressure on the olfactory bulb or tract, a larger volume of odor was necessary in order to pass the region of the block. In other words, the minimal olfactory index was elevated, but with the greater strength of the olfactory stimulus the impulse that reached the brain had normal strength. This was shown by the fact that olfactory fatigue was not prolonged. The results of pressure on the extracerebral olfactory pathways were similar to those found in direct pressure on the nerve in the nerve-muscle preparation.

Finally, Dr. Strauss asked why tumor within the substance of the frontal lobe produced both elevation of the minimal olfactory index and prolongation of homolateral fatigue. If the tumor is situated in the frontal lobe, it causes not only prolonged fatigue, because it is within the brain tissue, but a certain amount of pressure on the extracerebral olfactory pathways, so that the minimal olfactory index also becomes elevated.

Dr. Putnam's question cannot be answered at present. I have been making olfactory tests on many other intracranial lesions than tumor. A large experience will be necessary before one can state whether and, if so, to what degree intracranial growth can be differentiated from other lesions by the quantitative olfactory tests. I may say, however, that in the large majority of instances of intracranial disease not neoplastic in character, the olfactory pattern is different from that found in association with tumor. In the patients who were referred for olfactory tests, the presence of tumor was known, a new growth was suspected or the existence of other intracranial disease—vascular, inflammatory, etc.—was recognized. In most instances the tests were made without any knowledge of the

symptoms from which the patient suffered or the clinical diagnosis that had been made. In a considerable number of instances, I was able, from the results of the olfactory tests, to state that the patient had a localized lesion in one or another portion of the brain and to add that if the disease was a tumor the growth was in one or the other definite location.

Furthermore, in a number of instances the olfactory tests failed to show a localized lesion, and most of the patients did not have a new growth. There was a group of patients with papilledema and other signs of increased intracranial pressure—conditions such as serous meningitis—in whose cases the tests allowed one to conclude that there was no localized lesion.

It is surprising and interesting that in a number of instances of vascular lesion in which the patient had hemiplegia the olfactory pattern as far as the minimal olfactory index and the duration of fatigue were concerned was normal. I am unable to say in how many instances this was found. A large experience is necessary, therefore, before one is justified in making any statement regarding the value of the tests not only for localization but for diagnosis. It is possible that the future will show that the tests may be of considerable value both for the localization of tumor of the brain and for the differentiation of tumor and other intracranial diseases.

PROSTIGMIN IN THE TREATMENT OF MYASTHENIA GRAVIS AND MUSCULAR DYSTROPHY

RESULTS OBTAINED WITH DIVIDED DOSES

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AND
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The treatment of myasthenia gravis has advanced remarkably in the past five years. Changes in therapy have kept pace with a better understanding of the mechanism of the transmission of excitation, with particular reference to the region of the myoneural junction. Our interest in this has been enhanced by the introduction of prostigmin,[1] (the dimethylcarbamic ester of 3-hydroxyphenyltrimethylammonium methylsulfate), an analog of physostigmine. Walker[2] in 1934 first described a case of myasthenia gravis in which the use of physostigmine resulted in definite improvement. In the following year she[3] demonstrated the dramatic temporary relief of symptoms in two patients with myasthenia gravis to whom prostigmin was administered. Since Walker's original observations, others[4] have given testimony to the

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1. The product has been introduced by Hoffmann-La Roche, Inc., Nutley, N. J., who donated the supply used in this study. The Council on Pharmacy and Chemistry of the American Medical Association has not as yet accepted the product.

2. Walker, M. B.: Treatment of Myasthenia Gravis with Physostigmine, Lancet **1**:1200-1201 (June 2) 1934.

3. Walker, M. B.: Case Showing the Effect of Prostigmin on Myasthenia Gravis, Proc. Roy. Soc. Med. **28**:759-761 (April) 1935.

4. (*a*) Pritchard, E. A. B., and Walker, M. B.: The Effect of Prostigmin on the Symptoms and on the Myogram in Myasthenia Gravis, J. Physiol. **84**:35-36 P, 1935. (*b*) Hamill, P., and Walker, M. B.: The Action of "Prostigmin" (Roche) in Neuro-Muscular Disorders, ibid. **84**:36-37 P, 1935. (*c*) Laurent, L. P. E.: Clinical Observations on the Use of Prostigmin in the Treatment of Myasthenia Gravis, Brit. M. J. **1**:463-465 (March 9) 1935. (*d*) Hamill, P.: Further Uses of Prostigmin, Lancet **1**:575 (March 9) 1935. (*e*) Verbiest, H.: Prostigmin in Therapy of Myasthenia Gravis, Nederl. tijdschr. v. geneesk. **79**:4372-4374 (Sept. 14) 1935. (*f*) Lindsley, D. B.: Myographic and Electromyographic Studies of Myasthenia Gravis, Brain **58**:470-482, 1935. (*g*) Everts, W. H.: The Treatment of Myasthenia Gravis by the Oral Administration of Prostigmin, Bull. Neurol. Inst. New York **4**:523-530 (Dec.) 1935. (*h*) Marinesco, G.; Sager, O., and Kreindler, A.: Recherches sur l'action de la prostigmine dans la myasthénie, Rev. neurol. **65**:416-421 (Feb.) 1936.

efficacy and mode of action of prostigmin in the treatment of myasthenia gravis.

In a study of the chemical processes which accompany activity and recovery in the myasthenic muscle, Nevin [5] concluded that they differ in no significant way from those which are characteristic of healthy muscle. He also pointed the investigative finger to the region of the neuromuscular junction as the most likely place in which to discover the clue to the proper understanding of the etiology and treatment of myasthenia gravis.

The work of Dale and Feldberg [6] indicated that the liberation of acetylcholine is concerned with the normal excitatory transmission at the myoneural junction.

Feldberg and Vartiainen,[7] in experimental work with the sympathetic ganglia, found that when potassium chloride and physostigmine are added to perfusing solutions, each increases the effectiveness of acetylcholine—potassium chloride by 50 per cent and physostigmine from eight to twenty times. This may explain the greater effectiveness of prostigmin as compared with that of potassium chloride in the treatment of myasthenia gravis.

Pritchard,[8] in myographic studies, showed a return to the normal myogram after the injection of prostigmin in patients with myasthenia gravis. Lindsley,[4f] with some modifications in the myographic observations, corroborated Pritchard's findings in essence and, in addition, in a study of the action potentials in cases of myasthenia gravis, noted a return to the normal electromyographic curve after the injection of prostigmin. Marinesco, Sager and Kreindler,[4h] in their studies on myasthenic patients with the plethysmograph, chronaxia and myograph, showed a restoration of the normal response following the use of prostigmin.

The accumulated evidence from physicochemical studies seems to indicate that prostigmin prevents or delays the destruction of acetylcholine by the choline esterase present in the blood and that acetylcholine or a related choline ester is concerned with the transmission of excitation from the somatic motor nerve endings to voluntary muscle.

In the cases recorded in the literature except the two reported by Everts,[4g] in which the oral administration of 90 mg. of prostigmin

5. Nevin, S.: Study of Muscle Chemistry in Myasthenia Gravis, Brain **57:** 239-254 (Oct.) 1934.

6. Dale, H. H., and Feldberg, W.: The Chemical Transmission of Secretory Impulses to the Sweat Glands of the Cat, J. Physiol. **82:**121-128, 1934.

7. Feldberg, W., and Vartiainen, A.: Further Observations on the Physiology and Pharmacology of a Sympathetic Ganglion, J. Physiol. **83:**103-128, 1934.

8. Pritchard, E. A. B.: "Prostigmin" in the Treatment of Myasthenia Gravis, Lancet **1:**432-434 (Feb. 23) 1935.

daily yielded gratifying results, the mode of administration of prostigmin and its dosage have remained essentially the same as those advocated by Walker [3] and Pritchard,[8] namely, intramuscular injections of single large doses of from 3 to 5 cc. of a 1:2,000 solution (from 1.5 to 2.5 mg.) combined with atropine sulfate once a day or at intervals of several days. When large doses were given, atropine had to be used to counteract the sometimes severe intestinal cramps and annoying bradycardia which ensued.

Despite the truly dramatic response of patients with myasthenia to prostigmin within a few minutes, the evanescent effect of the drug when given once daily, even in large doses, leaves the patient in almost the same state as before the injection. The influence of prostigmin wears off within from two to five hours, and thus rehabilitation of resistance to fatigue is not maintained, thereby preventing the patient from returning to normal activity.

With this one serious defect in an otherwise remarkable remedial agent, we have attempted to overcome the temporary effect of the drug by giving smaller doses two or, preferably, three times a day, in much the same manner as that in which insulin is used in diabetes.

REPORT OF CASES

CASE 1.—*History.*—M. E., a woman aged 32, single, who was first seen on Nov. 19, 1934, attributed her present condition to a fall twenty-one years before, when she had a mild nosebleed but was not rendered unconscious. One year after the injury she first noticed fatigue and weakness in the lower limbs after slight exertion. Blurring of vision occurred and was followed by gradual increase in the degree of weakness, until all four limbs were involved. Double vision appeared for the first time thirteen years prior to examination and had been intermittent since. There had been remissions and exacerbations. It was not until two months before the first examination that fatigability on talking, chewing and swallowing became manifest. There was also difficulty in keeping the eyes open.

Examination.—The patient was rather thin and her gait suggested a muscle dystrophy. Fatigability of the cranial musculature was evident. Ptosis of the eyelids was present bilaterally and was relieved with rest. In attempting to rise from the floor the patient climbed up on her legs in a typical dystrophic fashion. There was mild atrophy of the muscles of the shoulder and pelvic girdles. The tendon reflexes were present throughout and were equal on the two sides.

Course.—When given ephedrine and amino-acetic acid the patient improved for a time but not sufficiently to permit return to her household duties. Ephedrine and amino-acetic acid, however, became less effective with time. On Sept. 22, 1935, 3 cc. of prostigmin and $\frac{1}{100}$ grain (0.6 mg.) of atropine sulfate were given intramuscularly. Intestinal cramps resulted and an additional dose of $\frac{1}{75}$ grain (0.86 mg.) of atropine sulfate was given. There was marked improvement both subjectively and objectively within five minutes; the effect of the drug persisted for three or four hours, after which the patient again complained of ready fatigability. For the past few months she has injected 1 cc. (0.5 mg.) of prostigmin intramuscularly three times a day. She states that she is able to

carry on her daily tasks satisfactorily and does not experience the "let down" toward the close of the day that occurred when she was taking the single large dose. No atropine is given with the 1 cc. doses; even so, the patient does not complain of intestinal cramps or the distressing bradycardia she had with 3 cc. doses. There has been a notable improvement in all the myasthenic manifestations.

CASE 2.—*History.*—L. B., a man aged 61, who was seen first in 1931, became ill after an automobile accident in June 1930. He was unconscious for one hour and was in a hospital for eight days. Two months later the tonsils were removed and severe hemorrhage followed. Two weeks later he had diplopia, after which the left upper eyelid began to droop. The ptosis increased until the left eye was completely closed. He was studied at various hospitals and by many physicians in this country and abroad. The condition was diagnosed by some as neurosyphilis and by others as a posttraumatic state. In an effort to relieve the condition

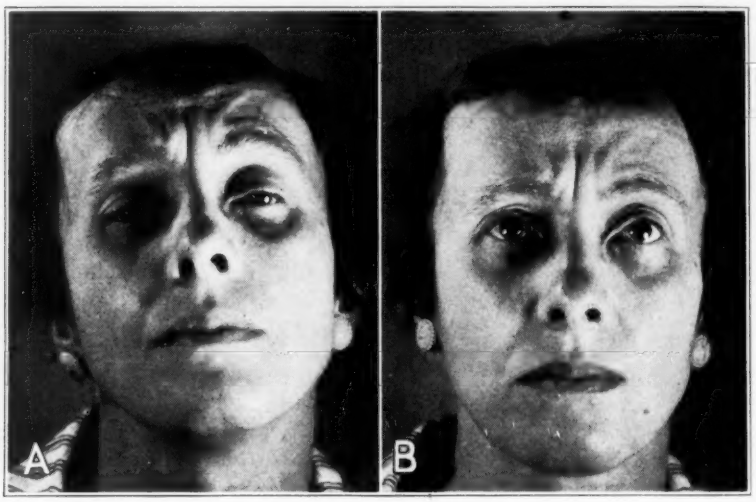

Fig. 1 (case 1).—Photographs of the patient: (*A*) prior to the injection of prostigmin, showing the typical myasthenic facies, with drooping of the upper lids, and (*B*) ten minutes after the injection of 2.5 cc. (1.5 mg.) of prostigmin.

various operations were performed. After an operation on the nasal sinuses there developed a bizarre deviation of the eyes. The diplopia varied from day to day. After the lapse of a year the left eye recovered completely, and a similar condition developed on the right side. The patient claimed that both eyes opened completely for a moment when he swallowed. At this time his condition was improved in the morning, but as the day passed ptosis of the right eyelid increased; by evening the right eye was closed. Slight exertion produced marked weakness, and he also had diplopia when the right eye was open. There was a period of remission, lasting one year. When he was seen in July 1935, the right eye was completely closed, and there was marked ptosis of the left upper eyelid. Diplopia was marked.

Examination.—The patient was robust. There was ptosis of both upper eyelids, of the right to such an extent as to close the eye. There was weakness of

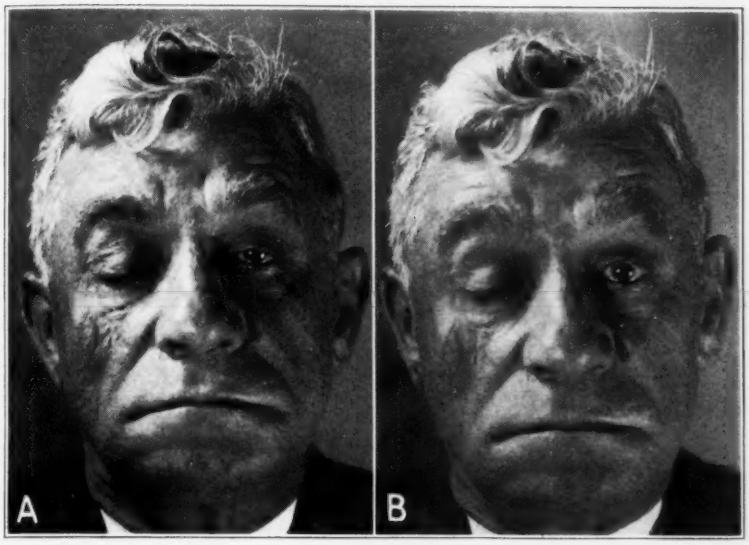

Fig. 2 (case 2).—Photographs prior to the use of prostigmin, showing (*A*) ptosis of both upper lids, with complete closure of the right eye, and (*B*) voluntary effort to raise the lids and elevate the eyes, resulting in only a partial increase in the size of the palpebral fissure on the left and no elevation of the right upper lid.

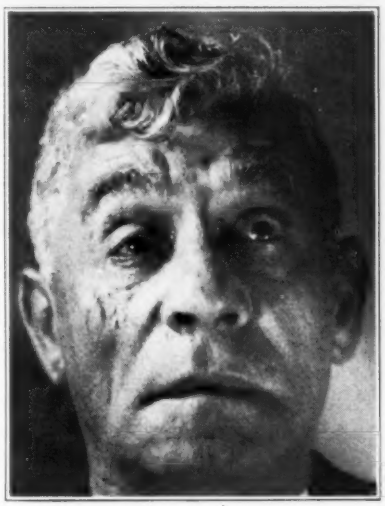

Fig. 3 (case 2).—Photograph of the same patient whose appearance prior to the use of prostigmin is seen in figure 2, showing the effect fifteen minutes after the injection of 3.5 cc. of prostigmin and 1/100 grain (0.6 mg.) of atropine sulfate. Both lids are elevated, and the right eye is about two-thirds open.

the ocular movements in all directions. He was unable to open the right eye voluntarily. When the right eye was held open diplopia occurred. Exertion produced ready fatigability.

Course.—Amino-acetic acid and ephedrine were used, both separately and together, for some time, without beneficial effect. On Sept. 11, 1935, 3.5 cc. of prostigmin and one-hundredth grain of atropine sulfate were given intramuscularly. Within three minutes the patient began to elevate the right lid, and the left palpebral fissure was perceptibly larger. He complained of severe intestinal

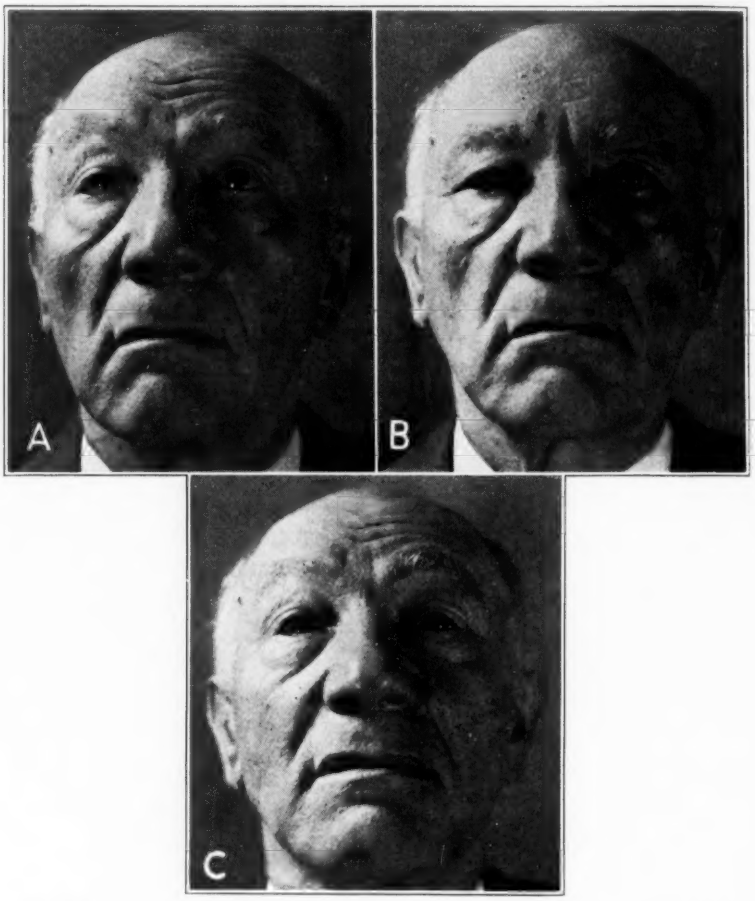

Fig. 4 (case 3).—Photographs showing (*A*) failure to develop the fold in the upper lids on voluntary effort to elevate the lids and (*B*) ptosis of the right lid prior to the injection of prostigmin. Even with effort the border of the right lid lies below the middle of the pupil and the border of the left between the limbus of the pupil and the periphery of the cornea. (*C*) was taken ten minutes after the injection of 3.5 cc. of prostigmin, showing the development of a fold in the upper lids and an increase in the size of the palpebral fissures, without attempt to elevate the lids.

cramps, a peculiar feeling in the epigastrium and a sensation of bulging of the eyes. The pulse rate, which formerly was 82, had dropped to 64 a minute. Another injection of one-hundredth grain of atropine sulfate was given. The right eye gradually opened until, after fifteen minutes had elapsed from the time of injection, the left eye was completely open and the right eye more than half open. When the right eye opened the patient complained of diplopia. Injections were given for two months, with improvement, particularly in the ptosis of the eyelids.

CASE 3.—*History.*—J. E., a man aged 70, married, who was seen first on June 25, 1936, had been ill for three months, during which diplopia occurred only at certain times of the day. He observed that on awakening in the morning both eyes were similar in size but that as the day progressed the right eye became smaller until at times it was almost closed. There never was difficulty in chewing or swallowing or body weakness.

Examination.—The patient was well preserved for his age. He had partial ptosis of the right eyelid and weakness of the left. There were no ocular palsies. Aside from moderate arteriosclerosis and rather low blood pressure, nothing unusual in the remaining physical examination was revealed.

Course.—Administration of ephedrine and amino-acetic acid had had no beneficial effect on his condition at any time. On Sept. 11, 1935, 3.5 cc. of prostigmin and one-hundredth grain of atropine sulfate were given intramuscularly. Five minutes after the injection the patient was able to lift both lids voluntarily to a greater extent than prior to the injection. He complained of severe cramps, faintness and a sense of tightness about the eyes. The pulse rate dropped from 72 to 60 a minute. An additional dose of atropine sulfate, one-hundredth grain, was given hypodermically. Twenty minutes later both eyes were open to within normal limits and they remained so for about four hours. The patient continued to suffer severe cramps and had a desire to defecate frequently. The unpleasant experience of cramps and faintness was sufficient for him to refuse to have further injections.

CASE 4.—*History.*—D. S., a woman aged 28, married, who was seen first on Feb. 17, 1936, complained of weakness for the preceding seven years. At first this was noticeable when she was dancing. On one occasion she fell to her knees in alighting from a street car. Two years after the onset she noticed gradual drooping of the eyelids, particularly when looking steadily at an object or a person. She had difficulty in talking because of rapid tiring of her lips. Diplopia made its appearance three years after the onset and has continued to the time of writing. There was considerable blurring of vision at times. Arthritis developed in November 1935. The tiredness was considered to be the result of focal infection, and in an effort to eradicate this the tonsils were removed in December 1935. After the operation the patient began to have difficulty in swallowing and talking, and the weakness in walking became intensified. She was unable to walk more than one or two blocks at a time. All symptoms were exaggerated preceding the menstrual cycle. Chewing and swallowing were accomplished with the greatest difficulty, and as a result, there was a marked loss of weight.

Examination.—The patient showed arthritic changes of the joints of both hands. She had the facies typical of myasthenia. There was bilateral ptosis of the eyelids. She tired readily after walking or talking. After any sustained effort the ptosis was increased. Speech became faint at times, and swallowing was accomplished with difficulty.

Course.—On Feb. 17, 1936, 2 cc. of prostigmin was given intramuscularly with one-hundredth grain of atropine sulfate. A remarkable subjective improvement was experienced within five minutes, and objectively the ptosis began to recede. Within thirty minutes the patient was able to sustain a conversation without tiring, and the difficulty in swallowing disappeared. Walking was considerably less tiring. Before using prostigmin the evening meal was an ordeal, followed by extreme exhaustion.

At the time of writing, the patient refuses to take three injections per day. She comes to the office daily for an injection at about 4 p. m. No matter whether 2 or 3 cc. of prostigmin is used, the relief lasts approximately three hours. Prior to the injection the patient is able to come to the office only by riding to within one block. After the injection she is able to walk home, a distance of ten blocks.

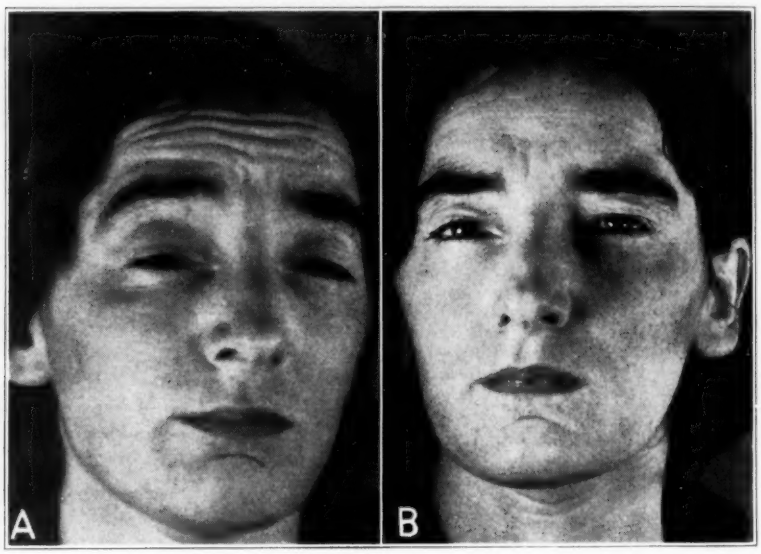

Fig. 5 (case 5).—Photographs showing (*A*) that even with extreme effort the patient was unable to elevate the lids more than 1 or 2 mm. and the normal folds were absent and (*B*) that seven minutes after the injection of 2.5 cc. of prostigmin the patient's expression became alert; both upper eyelids were elevated, and the normal folds were restored. The patient got up from bed immediately and walked for one-half hour after the injection, whereas prior to the injection she was unable to cross the room.

Case 5.—*History.*—A. F., a woman aged 22, single, who was confined to the Moss Home of the Jewish Hospital, dated the onset of her condition to the beginning of the menstrual cycle, at the age of 12½ years. The first symptoms were rapid exhaustion and drooping of the lids, particularly toward the end of the day. Gradual progression in the symptoms occurred, until the patient became practically unable to walk more than one-half block. Complete ptosis occurred. She had been in the Moss Home for three or four years prior to examination, being out of bed only part of the day. All symptoms increased

in intensity during the menstrual cycle. Aside from premenstrual pain, there were no difficulties with the menstrual function. It is interesting that the patient's sister had a similar condition prior to the removal of a large ovarian tumor.

Examination.—The patient was small and poorly nourished. Her gait was slow and waddling. She tired easily. She had an expressionless face, with drooping of the lids, and slowness and weakness of speech. The cranial nerves showed only a tendency to rapid exhaustion, which was relieved temporarily after a few minutes of rest. The reflexes were active and equal on the two sides. There were no abnormal reflexes. Sensation was intact.

Course.—In the hospital various forms of treatment were used. Amino-acetic acid and ephedrine were used separately and together, with little or no improvement. Intramuscular injection of extract of adrenal cortex gave definite improvement, but this was only temporary. In view of the history of improvement in the sister after the removal of an ovarian tumor, a pelvic examination was made and revealed normal results. Theelin was given, however, to see if it would produce a favorable response. There was no improvement. Prostigmin is now being used. After the first intramuscular injection of 2.5 cc. with one-hundredth grain of atropine sulfate, marked improvement occurred. With smaller doses of prostigmin without atropine sulfate, given twice daily, the patient shows a definite response.

CASE 6.—*History.*—M. M., a woman aged 34, married, who was seen first on Oct. 3, 1935, had first complained of "a weight in the back of the neck" during the early part of 1933. This sensation occurred at intervals. In October 1934 she began to complain of tiredness and weakness of the legs, particularly after walking a distance. This was followed shortly by the appearance of double vision, and in December 1934 drooping of the eyelids appeared. Speech was slow and thick, and difficulty in swallowing had been more or less constant. Chewing was difficult, and on a number of occasions fluids were regurgitated through the nose. Recently both upper limbs became weak. The patient complained of dizziness at times. There had been a loss of 40 pounds (18.1 Kg.) in weight since the onset of the condition. Symptoms of the bulbar type were accentuated with activity; in the early morning she was often free from symptoms. She had been using ephedrine and amino-acetic acid for some time, with indifferent results.

Examination.—The patient was fairly well developed. She showed the immobile facies typical of myasthenia. There was ptosis of both upper eyelids, the ptosis on the right being more marked than that on the left. The eyes were moved rather slowly and were not given full excursion. She was unable to elevate the eyes above the horizontal axis. The movements of the mouth were weakly executed, and the tongue was feebly protruded. The speech was thick and feeble and had a nasal twang. She had difficulty in swallowing solids. There was impaired strength in the upper and lower extremities. Walking the length of the room caused considerable fatigue. The reflexes were present throughout and equal on the two sides.

Course.—On Oct. 4, 1935, 3.5 cc. of prostigmin and $\frac{1}{75}$ grain (0.86 mg.) of atropine sulfate were given intramuscularly. After three minutes the patient was able to raise the eyelids and stated that swallowing was much easier. Within seven minutes the eyes were opened considerably, and she experienced a "lifting" sensation and return of strength. Speech was perceptibly improved ten minutes after the injection. There was a moderate increase in peristalsis and slight

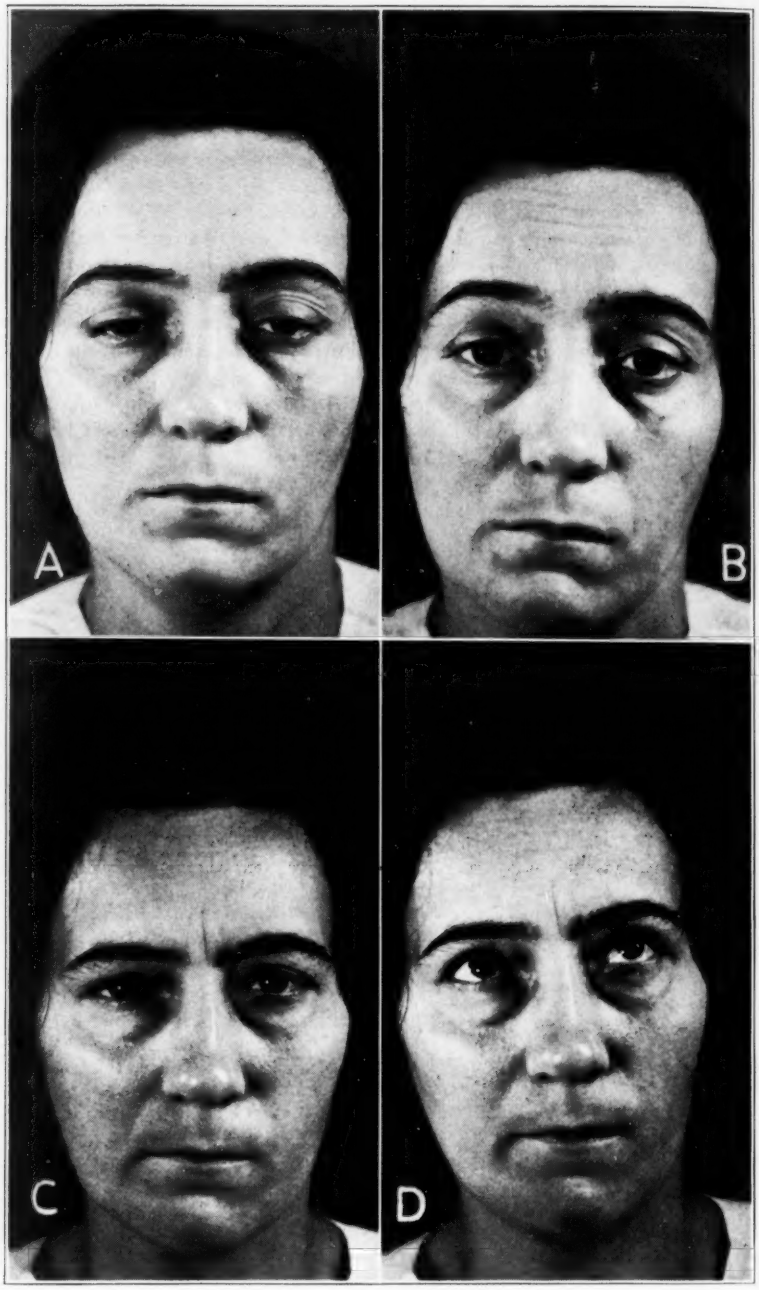

Fig. 6 (case 6).—Photographs showing (*A*) bilateral ptosis of the upper lids, more marked on the right; (*B*) voluntary effort to raise the lids and elevate the eyes above the horizontal axis, resulting in failure and producing the "woe-begone" appearance of myasthenia; (*C*) the normal fold in the upper lids and the alert appearance ten minutes after the injection of 3.5 cc. of prostigmin and $\frac{1}{75}$ grain (0.86 mg.) of atropine sulfate, and (*D*) voluntary effort to raise the eyes, resulting in elevation of the orbits above the horizontal axis. Lateral movements of the eyes were also more readily performed, and the excursion was greater.

faintness, as well as a sensation of bulging of the eyes. The pulse rate dropped from 86 to 70 for about ten minutes. She felt considerably strengthened for three hours after the injection. The ocular movements were of greater amplitude, and vertical movements particularly were improved. She now receives two injections daily of 1 cc. of prostigmin. In conjunction with this are given ⅜ grain (24.3 mg.) of ephedrine sulfate twice a day and 5 Gm. of amino-acetic acid three times a day. Ephedrine and amino-acetic acid are not as effective alone; prostigmin must be given to obtain satisfactory amelioration of symptoms. She is able at present to chew and swallow food without difficulty and has gained weight. Moreover, she can perform household duties that were formerly impossible.

Hamill,[4d] Hamill and Walker[4b] and Everts[4g] have reported the favorable action of prostigmin in various neuromuscular disorders. The following cases are reported of six patients with muscular dystrophies and one patient with amyotrophic lateral sclerosis to whom prostigmin was administered.

Case 7.—*History.*—C. K., a boy aged 9 years, who was seen first on Nov. 6, 1934, was the oldest of three children. At the age of 3 years there was noticed difficulty in walking, climbing stairs and arising from a recumbent position. This became progressively worse. At present he has a waddling gait, and the picture is typical of advanced pseudohypertrophic muscular dystrophy.

Course.—Amino-acetic acid, from 10 to 30 Gm., was given three times a day alone and in conjunction with ephedrine sulfate, without benefit. In October 1935 prostigmin in doses of 3 cc. was given intramuscularly. No cramps or untoward symptoms were experienced. No change was noted in the patient's condition. After the first injection the drug was given twice a day in doses of 1 cc., without atropine sulfate. After two months of therapy no improvement was noted.

Case 8.—*History.*—R. K., a boy aged 3 years, a brother of C. K. (case 7), who was seen first in December 1934, had shown beginning difficulty in climbing stairs and in arising from the recumbent position at the age of 1½ years. The gait and examination of the muscles of the calves and pelvic girdle revealed a picture typical of pseudohypertrophic muscular dystrophy in an early stage.

Course.—Amino-acetic acid was used from December 1934 to October 1935 in doses varying from 10 to 30 Gm. three times a day without appreciable benefit. Prostigmin was first used in October 1935, 2 cc. with 1/250 grain (0.26 mg.) of atropine sulfate being given intramuscularly, without any untoward effects. The pulse was not perceptibly slowed, and no cramps were experienced. The patient has received a daily dose of 1 cc. and has shown improvement in the following respects: he seems stronger; he arises from the recumbent position more rapidly; he does not tire as readily, and the gait has improved.

Case 9.—*History.*—R. M., a boy aged 12 years, who was seen first in July 1934, had had trouble in walking at the age of 1 year. He experienced difficulty in arising from the floor and in walking up the stairs. He had had a waddling gait up to two years before he was seen. He easily became tired and at the age of 10 years was unable to walk or stand. The condition became progressively worse, and there was loss of body weight.

Examination.—The boy was unable to move the lower extremities, and there was atrophy of the muscles of the shoulder and pelvic girdles. The tendon reflexes were absent. The picture was that of an advanced stage of pseudohypertrophic muscular dystrophy.

Course.—Amino-acetic acid administered from July 1934 to October 1935 produced no improvement. Prostigmin in doses of 3 cc. combined with $\frac{1}{200}$ grain (0.3 mg.) of atropine sulfate was given intramuscularly twice a week. The patient tolerated the large dose well, no cramps or marked bradycardia being noted. Since November 1935 he has received the drug in doses of 1 cc. twice a day without atropine sulfate. There has been a marked gain in weight and a distinct increase in strength. He can move both lower extremities freely but is still unable to stand unassisted.

CASE 10.—S. S., a youth aged 19, gave a history of typical pseudohypertrophic muscular dystrophy and presented a far advanced stage of the disease. Prostigmin given intramuscularly three times a day for one week in doses of 1 cc. produced no improvement in any respect.

CASE 11.—F. T., a man aged 21, had an advanced stage of scapulohumeral muscular dystrophy (Erb). Amino-acetic acid and ephedrine sulfate were administered, without benefit. Prostigmin given intramuscularly once a week in doses of 3 and 5 cc. produced no favorable effects, even temporarily. No cramps or bradycardia of consequence followed the injections.

CASE 12.—E. F., a woman aged 55, married, who was seen first on Nov. 27, 1935, had complained of weakness in the lower extremities since the age of 30. Her sister and two brothers, since the age of about 25 years, had similarly experienced weakness in the lower limbs and ready fatigability. They also had wasting of the muscles of the pelvic girdle and thighs. The patient's gait was that seen in muscular dystrophy, and she had the typical manner of arising from a recumbent position on the floor. The reflexes in the lower extremities were absent.

Course.—The patient has received prostigmin, 1 cc. three times a day. There has been a remarkable improvement in strength, and she is able to walk distances and perform work hitherto impossible.

CASE 13.—H. F., a man aged 42, in 1933 experienced loss of power in the right hand. There was progressive motor dysfunction, associated with atrophy and fibrillations, but no bulbar symptoms.

Prostigmin was given intramuscularly in doses of 2 cc. combined with one-hundredth grain of atropine sulfate, at intervals of from three to five days for fifteen injections. There was a definite increase in the fibrillary movements of the muscles, but no change was noted in muscular power or the neurologic status.

COMMENT

The usual dose of prostigmin administered intramuscularly, as suggested by Walker,[3] Pritchard,[8] Hamill and Walker,[4b] Hamill [4d] and Verbiest,[4e] has been from 3 to 5 cc., given in a single injection a day. Prostigmin has an influence on the cardiovascular system and the gastro-intestinal tract, as shown by Donatelli [9] Meneghini,[10] Chiatel-

9. Donatelli, L.: L'azione della prostigmina sull'apparato cardiovascolare, Arch. di sc. biol. **21**:201-212 (April) 1935.

10. Meneghini, T.: Contributo alla farmacologia della muscolatura liscia: Azione della prostigmina sull'utero e sull'intestino, Ann. di ostet. e ginec. **57**:665-678 (May 31) 1935.

lino[11] and Carmichael, Fraser, McKelvey and Wilkie.[12] We have found that even with the smaller dose of 3 cc. (1.5 mg.) adults complain of intestinal cramps with nausea and frequently of a sensation of faintness and bulging of the eyes. It appears that the greater the age of the patient the more marked are these complaints. Thus, the patient aged 70 (case 3) had pronounced cramps and bradycardia, despite the use of a large dose of atropine sulfate; the patient aged 61 (case 2) likewise had distressing symptoms of cramps and faintness; the other adult patients all had, to a greater or less degree, similar disturbing sensations when the single large dose was administered, with or without atropine sulfate. The untoward effects were distinctly less marked in children (cases 7, 8 and 9) and young adults (cases 10 and 11).

These untoward symptoms can be and are entirely eliminated when the drug is given in doses of 1 cc. (0.5 mg.) two or three times a day; moreover, the beneficent effects of the drug are prolonged throughout the waking hours, permitting useful activity and the taking of food. In cases 4, 5 and 6 the patients had difficulty in chewing and swallowing. When bulbar manifestations become marked crises may occur and result in death. Here prostigmin may act as a life-saving agent. The patients have made pronounced gains in weight as the result of better chewing and swallowing incident to the use of prostigmin.

It is of interest that the majority of the patients with myasthenia had received ephedrine or amino-acetic acid or both for an extended period, without any appreciable improvement. This is not altogether in accord with the observations of Edgeworth,[13] Boothby[14] and Tripoli, McCord and Beard.[15]

The results obtained in cases of muscular dystrophy indicate that in the early stage of the disease some improvement may be expected or even an arrest of symptoms obtained. It is too early to gage the effect of the drug, as in the case of the child aged 3 (case 8), but apparent improvement has occurred. Measurable improvement has

11. Chiatellino, A.: Documentazione radiografica dell'attivita di un nuovo enterocinetico, Gior. med. d. Alto Adige **6**:729-734 (Oct.) 1934.

12. Carmichael, E. A.; Fraser, F. R.; McKelvey, D., and Wilkie, D. P. D.: The Therapeutic Action of Prostigmin, Lancet **1**:942-945 (May 5) 1934.

13. Edgeworth, H., in discussion on papers by W. M. Boothby and J. G. Reinhold and others, J. A. M. A. **102**:267 (Jan. 27) 1934; A Report of Progress on the Use of Ephedrine in a Case of Myasthenia Gravis, ibid. **94**:1136 (April 12) 1930.

14. Boothby, W. M.: Myasthenia Gravis: Effect of Treatment with Glycine and Ephedrine (Fifth Report), Proc. Staff Meet., Mayo Clin. **9**:593-597 (Oct. 3) 1934.

15. Tripoli, C. J.; McCord, W. M., and Beard, H. H.: Muscular Dystrophy, Muscular Atrophy, Myasthenia Gravis and Strabismus, J. A. M. A. **103**:1595-1600 (Nov. 24) 1934.

taken place in two other patients (cases 9 and 12). In three patients (cases 7, 10, 11), whose condition was advanced, no improvement of any character was noted.

Hamill and Walker [4b] reported increased motor power in cases of amyotrophic lateral sclerosis following the use of moderate doses of prostigmin. The patient studied by us failed to respond favorably but did show a marked increase in the fibrillary movements of the affected muscles after injection of the drug.

SUMMARY AND CONCLUSIONS

Six patients with myasthenia gravis, six with muscular dystrophy and one with amyotrophic lateral sclerosis were treated with prostigmin for a period sufficient to gage its therapeutic value.

The effect of intramuscular injection of prostigmin in myasthenia gravis is noted within from three to five minutes, is maximal within one-half hour and gradually subsides after from three to five hours.

The administration of prostigmin in mild stages of myasthenia gravis results in complete relief of all clinical signs and symptoms; in more advanced forms relief is less complete but is still sufficient to warrant continuation of therapy.

In order to prolong the action of the drug over the entire day we have resorted to giving prostigmin in doses of 1 cc. three times a day, as is done with insulin. The result is to continue the improvement in muscular power during the patient's waking and active hours. This method of treatment with smaller doses obviates the untoward effect of single large doses given once a day, such as cramps, nausea and vomiting, a feeling of faintness and bulging of the eyes.

In the early stages of the muscular dystrophies the effect of the drug is to improve muscle power. Because of the slowness of the clinical course over many years, the effect of the drug must be studied for a prolonged period before conclusions can be drawn as to its clinical value.

The immediate result in cases of muscular dystrophy is to increase muscle power temporarily; in late stages with severe muscular atrophy and contractures no clinical improvement was noted.

In children the untoward effects of prostigmin are less intense or may be absent.

In one case of amyotrophic lateral sclerosis, treatment with this drug was followed by marked increase of the fibrillary tremors.

DISCUSSION

DR. P. BASSOE, Chicago: I can corroborate what Dr. Moore said about the dramatic effect of prostigmin in the treatment of myasthenia gravis. For the last two months I have had a patient with severe myasthenia gravis under observation. The immediate action of the drug was dramatic, but the effect passed off in from five to six hours.

There are two things that have interested me: One is the possibility of building up gradual improvement without increasing the dose, and the second, the substitution for the injection of a tablet taken by mouth. This patient, who received not increasing but decreasing doses, first by hypodermic injection and then by mouth, beginning a month before the time of this report, has improved and has received only two doses a day, given half an hour before the noon and the evening meal. Formerly, she could not chew and had to push her jaw up as she talked. Now she eats without difficulty. The effect of the drug carries over the night; so she is able to eat breakfast, and it does not begin to wear off to any extent until in the forenoon. It seems to me that the oral administration is equally effective, but it takes a little longer before the maximum effect is obtained—perhaps fifteen minutes, as compared with five minutes with the hypodermic injection. Aside from this, the effect seems to be equally good.

DR. J. F. FULTON, New Haven, Conn.: Do you give atropine with this drug?

DR. P. BASSOE, Chicago: One does not need to give atropine with the tablet because it has a different composition. I think a little atropine is incorporated in it.

DR. C. K. RUSSEL, Montreal, Canada: I can corroborate the statement regarding the dramatic effects of prostigmin in cases of myasthenia gravis. It was an exciting experience to see the reaction of a patient who was brought in in a condition of acute respiratory crisis. His disease had already lasted for three or four years. He could not close his eyes, had difficulty in swallowing and could not speak above a whisper or raise his arms above the level of his shoulders, and scarcely to that level. Fifteen minutes after I gave him a dose of prostigmin, he could talk well and quite loudly; he could close his eyes perfectly; he could swallow easily without trouble, and when he was told to raise his arms, they shot up with the extra effort he had been accustomed to make to move them at all. I found that a hypodermic injection of 0.5 cc. worked well to accomplish that result. Of course, this man was very ill with his respiratory crisis and difficulty in breathing. It was disappointing that, while the effect lasted for four or five hours, there resulted what seemed to be a decided let-down, and he was not nearly so well after the injection; so I felt hesitant about repeating it more often than was necessary. I had to put him in the Drinker respirator, and the use of the respirator and the drug was continued for several days, but he finally died. The let-down about five or six hours after the administration of the prostigmin seemed to me a serious disadvantage; otherwise it is a wonderful drug.

DR. ROBERT S. SCHWAB, Boston: I should like to make two comments. In using prostigmin in the treatment of progressive muscular atrophy and dystrophy with bulbar symptoms, Dr. Henry Viets and I observed only questionable improvement, compared with the dramatic changes noted in myasthenia gravis.

Because of this we felt that the drug could be used in establishing the diagnosis of myasthenia gravis when the presence of other conditions was suspected. We made a simple chart on which we could tabulate our results, so that we could get a quantitative evaluation of the effect of the drug on which to base the diagnosis. The results in myasthenia gravis were dramatic, appearing from ten to fifteen minutes after the injection of the drug and lasting several hours.

By adding the diagnostic values obtained by several observations, we found that in cases of myasthenia gravis the total was between 30 and 45, whereas in the dystrophies and in other diseases the values were always less than 10. The details appear in our paper (*New England J. Med.* **213**:1282 [Dec. 26] 1935).

I wish also to report here our attempt to confirm the work of Walker and Denny-Brown in using prostigmin by mouth. We administered, as they did,

⅛ grain (8.1 mg.) by mouth preceded by 15 minims (0.924 cc.) of tincture of belladonna. In four cases in which we tried it the results were discouraging. There was no evident improvement. The patients were uncomfortable, complaining of pain in the chest and abdomen and of tinnitus, vertigo and nausea. Although we increased the amount of tincture of belladonna administered with the drug, we did not get such results as were reported in the British journals.

In the same cases we obtained dramatic results with the injection of prostigmin subcutaneously, as has been described here.

Dr. A. W. Morrison, Minneapolis: Have studies on the myasthenic reaction been made, and if so, what changes occurred?

Dr. M. T. Moore, Philadelphia: Dr. Bassoe has brought up an extremely important point, the administration of the drug prior to meal-time. A number of patients have exceeding difficulty in eating. As a matter of fact, what is ordinarily an enjoyable procedure becomes an ordeal for them, and the administration of the drug prior to meal-time permits them to masticate their food properly and actually to enjoy the taking of food.

Everts has reported the use of prostigmin orally in three cases and has noted rather gratifying results. However, there are several things to be considered in the oral administration of the drug. First, it is essential to give about 90 mg. per day in order to get the desired effect. The parenteral administration permits of the use of a total of from 1.5 to 2.5 mg. per day, and there is a considerable difference in cost to the patient. We have used the drug orally and have found that it is not as effective as by injection. The effect comes on within a period of from twenty to thirty minutes and does not last as long as the effect obtained by parenteral administration.

One patient whom I described insisted on returning to the use of the drug by the needle because she felt that it was not so effective when administered orally.

We do not use atropine when we give the drug in doses of 1 cc. As a matter of fact, when we give it to children it is not necessary to use atropine, even with doses as large as 3 cc. It seems that the parasympathicotonic effect of the drug is not so marked in children as in adults.

Dr. Russel spoke of a case in which respiratory crises and a subsequent let-down followed the use of the drug. We have noted in the cases in which the condition was severe a tendency for a temporary let-down. However, if the drug is pushed, we find that the let-down does not persist and that in the late stages it might not be amiss to use amino-acetic acid in conjunction with prostigmin, particularly in cases in which there is marked involvement of the muscles of respiration and deglutition.

Dr. Schwab pointed out the value of the use of the drug as a means of differential diagnosis. I believe that his point is well taken, and we also find that in cases in which the question arises as to whether the patient has myasthenia gravis or a dystrophy, the drug does serve a useful purpose as a diagnostic substance.

We have not performed any experiments for determining electrical reactions for these patients, but the work of Lindsley, Marinesco and their co-workers has shown that there is a return to normal in the response of the myasthenic patient after the injection of prostigmin. The work of Lindsley and of Pritchard with the myograph have indicated this. The action potentials apparently are restored to normal, as shown by Lindsley, and chronaxia and the myograph also show a return to the normal response, as shown by Marinesco.

Dr. C. K. Russel, Montreal, Canada: I can say that the myasthenic reaction as shown by the knee jerk disappears after the injection of prostigmin.

GENICULATE NEURALGIA (NEURALGIA OF THE NERVUS FACIALIS)

A FURTHER CONTRIBUTION TO THE SENSORY SYSTEM OF THE FACIAL NERVE AND ITS NEURALGIC CONDITIONS

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It is thirty years since I made my first report to the American Neurological Association on herpetic inflammation of the geniculate ganglion and geniculate neuralgia.[1] This subject I elaborated in some detail in a series of subsequent publications.[2] Up to that time the facial nerve in man had been regarded as essentially motor; its sensory system —the nerve of Wrisberg and the geniculate ganglion and its peripheral divisions—were accorded only secretory, vasomotor and gustatory functions.

Spiller,[3] however, had already drawn attention to the preservation of deep sensibility of the face in the anesthetic area after removal of the gasserian ganglion, which supported the hypothesis of Henry Head that motor nerves convey sensory fibers of deep sensibility. Cushing[4] also had indicated in his studies of the trigeminal field after operation on the gasserian ganglion the preservation of a crude form of tactile sensibility on the anterior two thirds of the tongue, probably of facial origin. Slight hypesthesia in the area of distribution of the chorda tympani nerve to the tongue after facial palsy had been noted as early

Read by title at the Sixty-Second Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 3, 1936.

1. Hunt, Ramsay: Herpetic Inflammation of the Geniculate Ganglion: A New Syndrome and Its Complications, J. Nerv. & Ment. Dis. **34**:73, 1907.

2. Hunt, Ramsay: (*a*) Otalgia Considered as an Affection of the Seventh Cranial Nerve, Arch. Otol. **36**:543, 1907; (*b*) A Further Contribution to the Herpetic Inflammation of the Geniculate Ganglion, Am. J. M. Sc. **136**:226, 1908; (*c*) The Sensory System of the Facial Nerve and Its Symptomatology, J. Nerv. & Ment. Dis. **36**:321, 1909; (*d*) The Symptom-Complex of Acute Posterior Poliomyelitis of the Geniculate Auditory, Glossopharyngeal and Pneumogastric Ganglia, Arch. Int. Med. **5**:631 (June) 1910; (*e*) The Sensory Field of the Facial Nerve (A Further Contribution to the Symptomatology of the Geniculate Ganglion), Brain **38**:418, 1915.

3. Spiller, W. G.: Deep Pressure Sensibility of the Seventh Nerve, J. Nerv. & Ment. Dis. **33**:736, 1906.

4. Cushing, H.: The Sensory Distribution of the Fifth Cranial Nerve, Bull. Johns Hopkins Hosp. **15**:213, 1904.

as 1876 by Bernhardt,[5] and in rare instances the observation had been confirmed by others.

Other slight sensory disturbances, viz., pain in the ear and anesthesia of the concha, which had been noted in cases of facial palsy, were regarded as of vagal or trigeminal origin. Apart from these isolated observations, the visceral and somatic sensory functions of the facial nerve had escaped notice, in spite of the progress which had been made in the knowledge of its motor, secretory and gustatory activities.

The opening wedge in the discovery of this small but important sensory system was the observation of the geniculate ganglion syndrome,

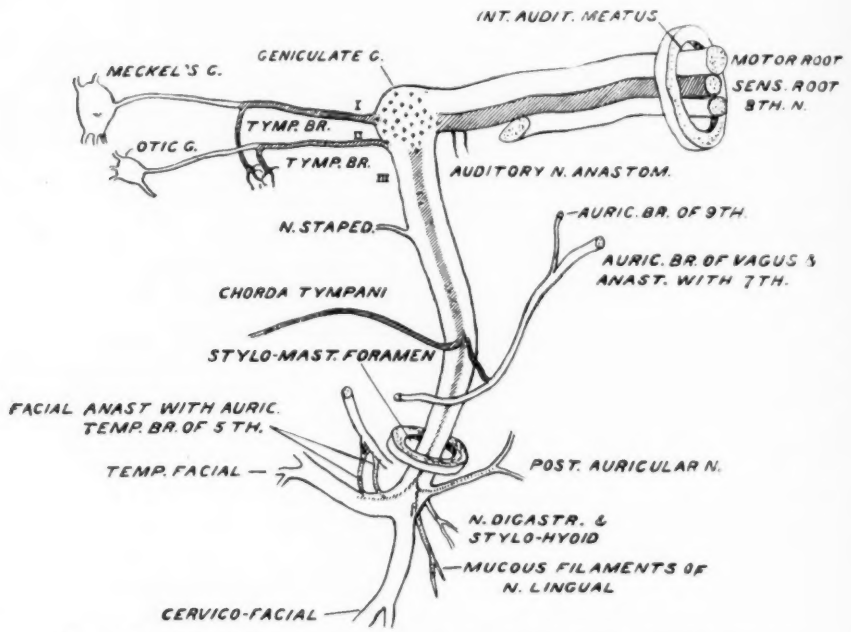


Fig. 1.—Diagrammatic representation of the facial nerve, showing the geniculate ganglion, the sensory root (nerve of Wrisberg) and the peripheral divisions. The sensory system is shaded (from Hunt[2e]).

which led to the following conclusions: The facial nerve in man has a definite sensory system, like the other mixed cranial nerves; the geniculate ganglion is composed of unipolar cells, the central processes of which terminate in the fasciculus solitarius of the medulla, with the central processes of the ninth and tenth nerves, and constitute its sensory root (fig. 1).

5. Bernhardt, M.: Krankheiten der peripherischen Nerven, in Nothnagel, C. W. H.: Specielle Pathologie und Therapie, Vienna, A. Hölder, 1895, vol. 11, p.183.

From the ganglion itself there arise the great and the small superficial petrosal nerve, which terminate in important ganglia of the cerebral portion of the sympathetic system (Meckel's ganglion and the otic ganglion). Both these petrosal nerves give off in their course descending branches which take part in the formation of the tympanic plexus; these descending branches are called the great and the small deep petrosal nerve.

The facial nerve proper, which courses within the fallopian aqueduct, includes, in addition to motor and chorda tympani fibers, sensory fibers, which spring from the cells of the geniculate ganglion. These sensory fibers (fig. 2) are somatic and are destined for the cutaneous distribution of the facial nerve on the external ear (zoster zone of the geniculate ganglion), the petrosal nerves and the chorda tympani nerve

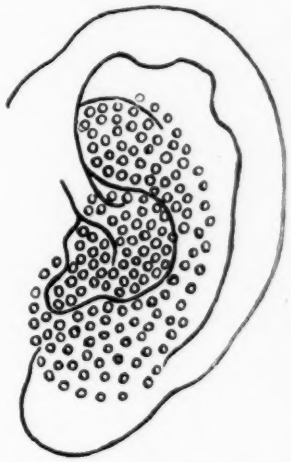


Fig. 2.—Diagrammatic representation of the cutaneous zone of innervation of the geniculate ganglion on the auricle, outlined by the herpes zoster method (from Hunt [2e]).

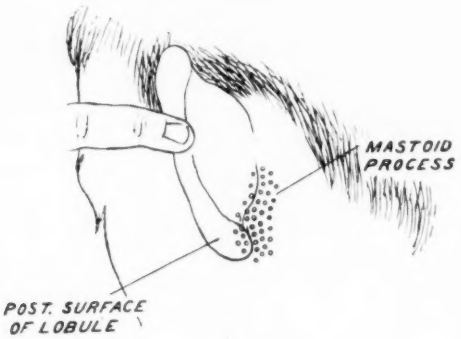
passing to the intra-oral field. This sensory system of the facial nerve participates in the innervation of the internal ear, the middle ear, the tympanum and the cutaneous zone of the external ear.

There was also evidence that a vestigial remnant of innervation persists in a strip on the posteromesial surface of the auricle (fig. 3*A*) and within the buccal cavity, in the area of distribution of the chorda tympani nerve, and on the palate, near the anterior pillar of the fauces (fig. 3*B*).

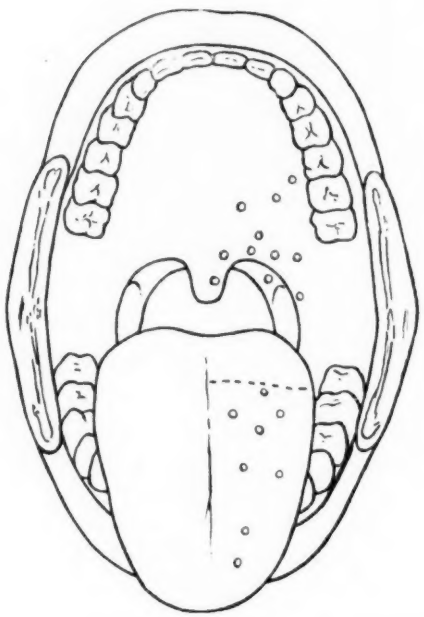
It was emphasized that this sensory system is vestigial and regressive, the representation in man of what in the lower vertebrates is a considerable sensory distribution to the vault of the palate, the tongue and the floor of the mouth.

In the realm of symptomatology, I considered the neuralgic conditions of the geniculate ganglion and the various types of the geniculate ganglion syndrome (herpetic ganglionitis).

In this presentation it is my purpose to review the anatomic features of the geniculate system in the light of advances which have been made



A



B

Fig. 3.—Diagrammatic representations (from Hunt[2e]) (*A*) of a cutaneous strip of innervation of the geniculate ganglion on the posteromesial surface of the auricle, outlined by the herpes zoster method, and (*B*) the distribution of the intra-oral remnants of the geniculate visceral sensory system on the palate and in the distribution of the chorda tympani nerve on the tongue, as determined by the herpes zoster method.

during the past twenty-five years and to rectify any errors and to indicate any advances which have been made in knowledge of this complex sensory field. The delimitation of such an obscure and intricate sensory system is rendered difficult by reason of its vestigial and variable nature. The subject has a special clinical interest because of its relation to geniculate neuralgia, which will be considered in subsequent sections of the paper.

SENSORY SYSTEM OF THE FACIAL NERVE

The facial nerve, in addition to its motor and gustatory functions, plays an important rôle in the innervation of the vasomotor and secretory activities of the lacrimal and salivary glands (sympathetic and parasympathetic fibers). In the present study only the somatic and visceral sensory systems will be considered.

SOMATIC SENSORY SYSTEM (CUTANEOUS FIELD OF THE GENICULATE GANGLION)

The somatic sensory innervation of the facial nerve in man had not been recognized prior to my description in 1907. With the use of the eruption of herpes zoster as a guide, it was possible, by analyzing a large number of cases of geniculate ganglionitis, to arrive at an approximate delimitation of its zoster zone (fig. 2). Within this area lies the cutaneous representation of the facial nerve, between the trigeminal nerve in front and the cervical nerves behind. The auricular branch of the vagus nerve and a small auricular branch from the glossopharyngeal nerve also participate in the innervation of this area. At the time of my first publication anatomic evidence indicated that the cutaneous fibers of geniculate origin reached their destination by way of the auricular branch of the vagus nerve (Arnold's nerve) or the posterior auricular branch of the facial nerve. The former nerve anastomoses with the facial nerve in the aqueduct of Fallopius and is then continued as a sensory branch of the external auditory canal and the posterior aspect of the auricle [6] (fig. 4).

Since that time a number of contributions have confirmed the existence of a cutaneous component in the facial nerve in man.

The relation of the auricular branch of the vagus nerve (sensory branch of the external auditory canal) and the posterior auricular nerve to the sensory innervation of the auricle has been carefully investigated

6. The auricular branch of the vagus nerve, after its anastomosis with the facial nerve in the aqueduct of Fallopius, is termed by some writers the sensory branch of the external auditory canal (*rameau sensitif du conduit auditif externe*).

by Hovelacque and Rousset,[7] with the use of the dissection method to determine the cutaneous distributions. In these two nerves they observed a marked tendency to anomaly and variation. When both nerves exist separately, they arise from the facial nerve after its exit from the stylomastoid foramen, and in the order named. Exceptionally the sensory branch to the auricle arises below the posterior auricular branch. In other instances both may be represented by a single nerve. Rarely there may exist three nerves, the posterior auricular nerve consisting of two branches.

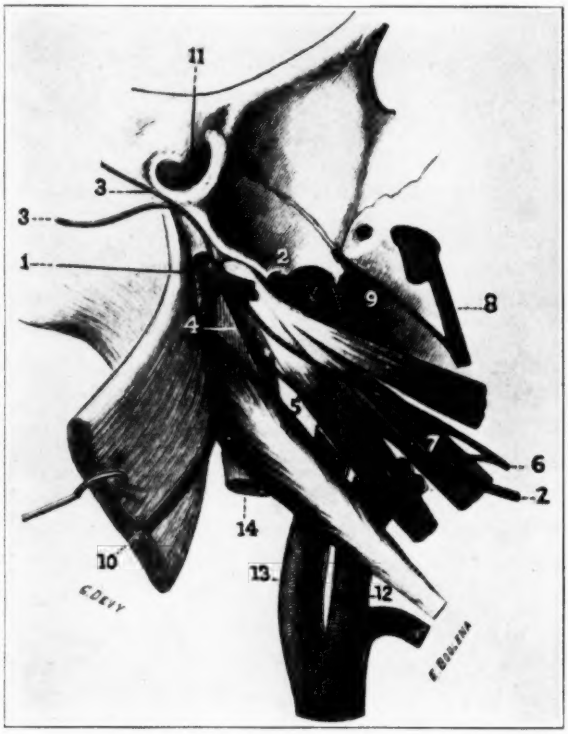


Fig. 4.—Drawing showing the extrapetrous branches of the facial nerve (from Testut and Latarjet[9]). *1* indicates the facial nerve; *2*, the glossopharyngeal nerve; *3*, the sensory branch of the external auditory canal, with the posterior auricular nerve just below; *4*, the nerve of the digastric muscle; *5*, the nerve of the stylohyoid muscle; *6*, the lingual branch; *7*, the anastomotic branch of the glossopharyngeal and lingual nerves; *8*, the lingual nerve; *9*, the chorda tympani nerve; *10*, the spinal accessory nerve; *11*, the external auditory meatus; *12*, the external carotid artery; *13*, the internal carotid artery, and *14*, the internal jugular vein.

7. Hovelacque, A., and Rousset, J.: Note sur la disposition anatomique de rameau sensitif du conduit auditif externe et du rameau auriculaire postérieur du facial, Bull. et mém. Soc. anat. de Paris **92**:318, 1922.

These observations show the great variability in the mode of origin and termination of these two nerves. Together they convey to the auricle and the external auditory canal the cutaneous filaments from the facial nerve, as well as cutaneous fibers from the auricular branches of the vagus and glossopharyngeal nerves. Here, in the somatic field as in the visceral, these three nerves are closely associated.

Quain [8] also commented on the great variability of Arnold's nerve (the auricular branch of the vagus nerve). He stated that in rare instances this auricular branch is absent. In other instances there is no communication with the facial nerve.

Occasionally the auricular nerve passes entirely into the trunk of the facial nerve, in which case its fibers are probably conveyed to the external ear through the posterior auricular nerve.

Testut and Latarjet,[9] in the last edition of "Traité d'anatomie humaine," described the sensory branch to the external auditory canal (*rameau sensitif du conduit auditif externe*) as terminating in the zoster zone of the geniculate ganglion.

> It supplies sensation to a portion of the auricle (the concha, tragus, antitragus, lobule and anthelix), the external auditory canal and a portion of the tympanum. This territory represents Hunt's zone of the geniculate ganglion and belongs to the system of the nerve of Wrisberg.

Later investigators have therefore confirmed my earlier view that cutaneous fibers of geniculate origin course in the trunk of the facial nerve and reach their destination by way of the auricular branch of the vagus nerve or the posterior auricular nerve.

Comparative neurology has also thrown light on this question. The existence of a sensory somatic component in fishes has long been recognized. Rhinehart,[10] however, in studies of serial sections of the head of the albino mouse, identified a cutaneous component of the facial nerve. He described a ramus cutaneus facialis, which emerges after the facial nerve is crossed by the auricular branch of the vagus nerve; the auricular branch of the vagus nerve and the facial sensory ramus then become intermingled, some of the fibers of each distribution passing out with the other nerve. The ramus cutaneus facialis terminates in the skin of the external auditory meatus and a portion of the auricle and possibly a part of the tympanic membrane. Rhinehart noted an admixture of fibers from the ramus auricularis vagi which are distributed with the cutaneous fibers of the facial nerve, as well as fibers from the facial

8. Quain, Jones: The Facial Nerve, in Schafer, E.; Symington, J., and Bryce, T. H.: Quain's Elements of Anatomy, ed. 11, London, Longmans, Green & Co., 1909, vol. 3, p. 42.

9. Testut, L., and Latarjet, A.: Traité d'anatomie humaine, Paris, Gaston Doin, 1930, vol. 3, p. 142.

10. Rhinehart, D. A.: The Nervus Facialis of the Albino Mouse, J. Comp. Neurol. **30**:81, 1919.

nerve which are distributed with the auricular branch of the vagus nerve. The ramus cutaneus facialis in the mouse is apparently represented in man by the ramus auricularis posterior. The two nerves in man and in the mouse are similar in origin and destination.

Larsell and Fenton [11] also demonstrated in a human fetus of 54 mm. the existence of a small cutaneous branch of the facial nerve corresponding closely to that described by Rhinehart in the mouse. The existence of a somatic component of the facial nerve in mammals, including man, has therefore been established, and this should settle any doubts which were raised as to its presence in the earlier history of the geniculate syndrome.

These investigations show that the somatic sensory component passes to the cutaneous field of the geniculate system by way of the sensory branch to the external auditory canal (auricular branch of the vagus nerve) and the posterior auricular nerve. There exists the greatest variation in these sensory filaments, which is in harmony with their vestigial nature. Somatic sensory fibers from the ganglia of the vagus and glossopharyngeal nerves are also distributed in the same area, so that the auricular branches of all three nerves, the seventh, the ninth and the tenth, are represented on the auricle in the geniculate zoster zone. This fact is of clinical importance, as the neuralgic conditions of all three nerves have associated otalgia.

VISCERAL SENSORY SYSTEM

The visceral sensory system of the facial nerve consists of two components: one passing to the intra-oral field and the other supplying deep sensibility of the face.

Intra-Oral Field of the Geniculate Ganglion.—In my original study the great and the small superficial petrosal nerve, the large and the small deep petrosal nerve and the chorda tympani nerve were all identified in part with the visceral sensory system of the facial nerve (fig. 1). Later investigations, however, showed certain limitations in respect to this sensory field.

The small superficial petrosal nerve and both deep petrosal nerves receive only parasympathetic fibers from the facial nerve and contain no visceral sensory fibers of geniculate origin. On the other hand, the great superficial petrosal nerve and the chorda tympani nerve both convey visceral sensory fibers from the geniculate ganglion to its intra-oral field. The innervation of the chorda tympani nerve, however, is essentially gustatory.

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11. Larsell, O., and Fenton, R. A.: The Embryology and Neurohistology of Sphenopalatine Ganglion Connections: A Contribution to the Study of Otalgia, Laryngoscope **37**:371, 1928.

Great Superficial Petrosal Nerve: Considerable advance has been made in knowledge of the origin, mode of termination and finer structures of the great superficial petrosal nerve (fig. 5). This nerve arises from the tip of the geniculate ganglion, passes through the hiatus Fallopii and traverses the middle fossa of the skull to the anterior lacerated foramen. There it is joined by the great deep petrosal nerve and is continued as the vidian nerve. The vidian nerve then passes through the vidian canal to Meckel's ganglion, on the second division of the fifth nerve. The great superficial petrosal nerve in its course through the middle fossa is extradural and stands in close relation to the pneumatic cells of the petrous bone. The vidian nerve, which courses in the pterygoid canal, is similarly exposed to infection by its proximity to the sphenoid and ethmoid cells.

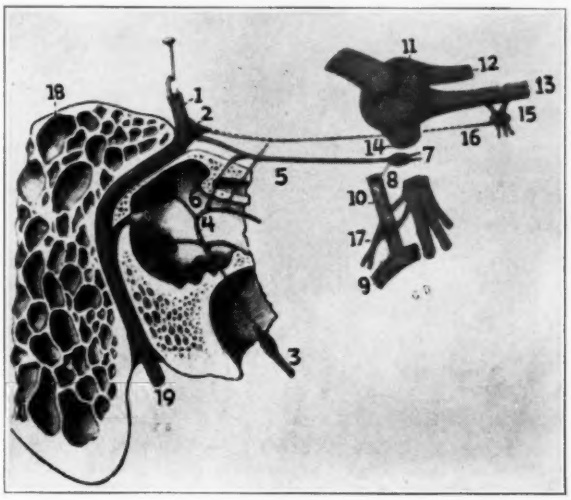

Fig. 5.—Drawing showing the facial nerve, the geniculate ganglion and the petrosal nerves (from Testut and Latarjet[9]). *1* indicates the facial nerve; *2*, the geniculate ganglion; *3*, the glossopharyngeal nerve; *4*, Jacobson's nerve; *5*, the small superficial petrosal nerve; *6*, the small deep petrosal nerve; *7*, the otic ganglion; *8*, the sympathetic root of the otic ganglion; *9*, the internal maxillary artery; *10*, the middle meningeal artery; *11*, the gasserian ganglion and its three branches; *12*, the ophthalmic nerve; *13*, the superior maxillary nerve; *14*, the inferior maxillary nerve; *15*, the sphenopalatine (Meckel's) ganglion; *16*, the great superficial petrosal or vidian nerve; *17*, the auriculotemporal branch of the fifth nerve; *18*, mastoid cells, and *19*, the great deep petrosal nerve.

The work of Larsell and Fenton[11] showed that the great superficial petrosal nerve contains both large and small myelinated sensory fibers, which originate in the cells of the geniculate ganglion. They also established the important fact that the large sensory fibers pass through the

sphenopalatine ganglion without interruption and join the posterior nasal and the palatine branch of this ganglion. By this pathway the geniculate ganglion stands in direct sensory relationship with the orbital, palatal and nasal branches of Meckel's ganglion and the maxillary division of the fifth nerve. This nerve is the homolog in man of the large palatine branch of the seventh nerve, which has so conspicuous a sensory innervation in lower forms and constitutes the so-called white ramus of Meckel's ganglion (fig. 6). It represents a neural pathway between the geniculate ganglion and the mucous membrane of the posterior palatal and posterior nasal regions.

According to Sheldon,[12] the possibility of a gustatory innervation should also be considered, as this palatine branch of the facial nerve in lower forms subserves both special and general sensibility.

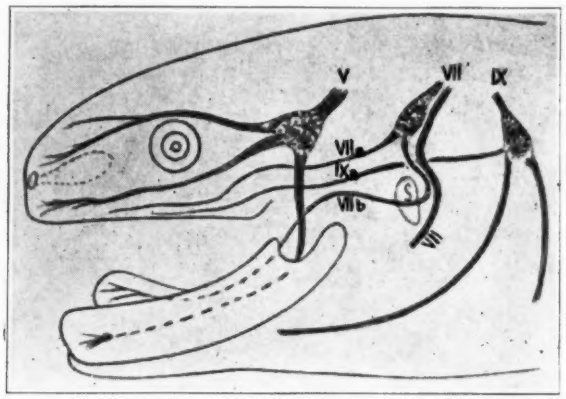

Fig. 6.—Drawing showing the distribution of the cranial nerves in a lower vertebrate form (from Wiedersheim, W.: Comparative Anatomy of Vertebrates, London, Macmillan & Co., 1907). *VII* indicates the facial nerve and the geniculate ganglion; *VII*^{a}, the Ramus palatinus; *VII*^{b}, the Ramus lingualis.

Great Deep Petrosal Nerve: This nerve, which joins the great superficial petrosal nerve to form the vidian nerve, is composed of fibers from the tympanic plexus and Jacobson's nerve. According to Müller,[13] the fibers of the deep petrosal nerve are nonmedullated, arising in the carotid plexus of the sympathetic nervous system. These fibers are postganglionic, arising in the superior cervical sympathetic ganglion, and constitute the so-called gray ramus of the sphenopalatine ganglion.

12. Sheldon, R. E.: The Phylogeny of the Facial Nerve and Chorda Tympani, Anat. Rec. **3**:593, 1909.

13. Müller, L. R.: Die Lebensnerven und Lebenstriebe, ed. 3, Berlin, Julius Springer, 1931, pp. 500 and 509.

Larsell and Burns,[14] however, demonstrated in the great deep petrosal nerve large afferent myelinated nerve fibers, which they ascribed to Jacobson's nerve (tympanic branch of the glossopharyngeal nerve) and which, like similar fibers arising in the geniculate ganglion, pass through the sphenopalatine ganglion to the palatal nerves. These glossopharyngeal fibers represent a remnant of the palatine branch of the glossopharyngeal nerve, which is so conspicuous in lower vertebrate forms. Here again, in the viscerosensory field as in the somatic, the facial and the glossopharyngeal innervation are closely associated.

Small Superficial Petrosal Nerve: This nerve is joined soon after its emergence from the geniculate ganglion by the small deep petrosal nerve and passes to the otic ganglion, on the third division of the fifth nerve at its bifurcation into the inferior dental and the lingual branch (fig. 5). The major portion of this nerve is received from the small deep petrosal nerve, which arises from the tympanic plexus and Jacobson's branch of the glossopharyngeal nerve. The fibers from the tympanic branch of the glossopharyngeal nerve (Jacobson's nerve) constitute the white ramus of the otic ganglion. The superior cervical ganglion of the cervical portion of the sympathetic trunk also participates in this innervation.

According to Larsell and Burns [14] and Müller and Dahl,[15] the branch from the geniculate ganglion which forms the small superficial petrosal nerve is wholly sympathetic and contains no large sensory fibers. It must therefore be regarded as subserving a vasomotor and secretory function.

These recent investigations on the petrosal nerves show that the great superficial petrosal nerve is an integral part of the geniculate visceral sensory system. The other petrosal nerves, the small superficial petrosal nerve and both deep petrosal nerves, are not a part of the geniculate system. These nerves receive their sensory supply from the tympanic branch of the glossopharyngeal nerve (Jacobson's nerve) and innervate the tympanic cavity and mastoid cells.

That the middle ear does not receive a sensory innervation from the seventh nerve is still further corroborated by the elaborate studies of Rhinehart on the facial nerve of the albino mouse; he observed no evidences of such an innervation in his series of sections. He did, however, demonstrate afferent fibers of geniculate origin in both the chorda tympani and the great superficial petrosal nerve. In addition to the special visceral afferent fibers in the chorda tympani nerve, there was also

14. Larsell, O., and Burns, E. M.: Some Aspects of Certain of the Cranial Nerves, Ann. Otol., Rhin. & Laryng. **40**:661, 1931.

15. Müller, L. R., and Dahl, W.: Die Beteiligung des sympathischen Nervensystems an der Kopfinnervation, Deutsches Arch. f. klin. Med. **99**:48, 1910.

evidence that this nerve contains afferent fibers conveying common sensation from the tongue, which is in harmony with the clinical findings already noted.

I wish to emphasize also the anatomic proof that the great superficial petrosal nerve has intimate associations with the maxillary division of the fifth nerve and participates in the innervation of the posterior palatal and the posterior nasal region and to indicate the bearing this may have on the distribution of pain in geniculate neuralgia, as well as the distribution of the eruption of herpes zoster in geniculate ganglionitis. In my original outline of the geniculate intra-oral zone, a distribution of vesicles was indicated in this region (fig. 3 *B*). Careful intranasal investigation in the future will probably show a similar eruption of herpetic vesicles in the posterior nares in association with geniculate ganglionitis.

VISCERAL SENSORY SYSTEM (DEEP SENSORY FIELD OF THE GENICULATE SYSTEM)

Another important component of the geniculate sensory field is deep sensibility of the face, which is represented in the afferent system of the peripheral branches of the facial nerve proper.

The existence of afferent fibers in the nerves of skeletal muscles was demonstrated by Sherrington [16] in 1894. He observed that from one third to one half of the myelinated fibers in the muscle nerves are sensory, originating in the spinal root ganglia and passing to the muscle spindles and other muscle nerve endings.

Head [17] and his co-workers in 1895 showed the relationship of these fibers to deep sensibility, viz., sensations of tactile and painful pressure, localization of deep touch and position of the parts in space. All these modalities of sensibility are associated with some aspect of pressure and are undisturbed by denervation of the skin.

In the realm of the facial nerve, Spiller and his associates Ivy and Johnson [18] were the first to indicate the preservation of this form of sensibility in the face after section of the trigeminal nerve. In accordance with the hypothesis of Head, they referred it to the existence of afferent fibers of deep sensibility in the seventh cranial nerve. These

16. Sherrington, C. S.: On the Anatomical Constitution of Nerves of Skeletal Muscles, J. Physiol. **17**:211, 1894.

17. Head, Henry: The Phenomena of Deep Sensibility, in Head, H., and others: Studies in Neurology, London, Oxford University Press, 1920, vol. 1, chap. 3, p. 246.

18. Ivy, R. H., and Johnson, L. W.: Preservation of Deep Sensibility of the Face After Destruction of the Fifth Nerve, Univ. Pennsylvania M. Bull. **20**:35 (May) 1907.

clinical observations were later confirmed by many observers, such as Maloney and Kennedy,[19] Kidd,[20] Souques,[21] Hartmann [22] and, notably, Davis [23] in 1923, whose clinical and experimental studies gave final proof of the existence of this deep visceral sensory system. Each of the patients in Davis' series on whom trigeminal neurectomy had been performed showed loss of superficial sensation corresponding to the accepted area of the trigeminal supply. In addition, all showed the definite presence of pressure pain sensation, and the algometer readings on the affected side were almost identical with those on the normal half of the face.

In addition, opportunity was afforded for the study of a case in which there was concomitant paralysis of the fifth and seventh cranial nerves on one side, and of another in which the same conditions were present over the ophthalmic division of the fifth nerve. In the first instance pain could not be produced with 15 Kg. of pressure over any point on the right half of the face, the side of the lesion. In the second case the same observation was made concerning the region over the forehead where the fifth and the seventh nerve supply was lost.

Souques,[21] in a case of retrogasserian section of the trigeminal nerve, also demonstrated complete loss of superficial sensation, with preservation of deep sensibility. The later development of palsy of the facial nerve on the same side was followed by loss of deep sensibility, which had existed before the palsy. These observations furnish conclusive demonstration of the existence of a deep sensory system of the face of facial nerve origin.

Davis' experiments, which were carried out on cats, showed that when the trigeminal root is completely cut or the ganglion thoroughly avulsed there is complete loss of response on the corresponding half of the face, the cornea and the mucous membrane of the nose and mouth to superficial stimulation with a strong, painful faradic current. However, if the sharp-pointed electrodes are thrust beneath the skin into the facial muscles or on to the bone and stimulation is induced, there is an unquestioned response. Further, if the facial nerve to the same side is cut, producing definite paralysis of the peripheral portion of the facial nerve, neither superficial nor deep faradization produces

19. Maloney, W. J., and Kennedy, F.: The Sense of Pressure in the Face, Eye and Tongue, Brain **34**:1, 1911-1912.

20. Kidd, L. J.: Lachrymal Reflexes: Pressure Sensibility of Head and Neck, Rev. Neurol. & Psychiat. **7**:167, 1909.

21. Souques, A.: Les fibres de la sensibilité profonde de la face; passent-elles par le nerf facial? Rev. neurol. **31**:86, 1924.

22. Hartmann, E.: Le neurotonie retro-gassérienne; ses conséquences physiologiques, Thèse de Paris, no. 134, 1924.

23. Davis, Loyal E.: The Deep Sensibility of the Face, Arch. Neurol. & Psychiat. **9**:283 (March) 1923.

a response. This is conclusive experimental evidence that muscle sensory fibers to the facial muscles are contained within the peripheral trunk of the facial nerve.

Gerard [24] in an experimental study of the afferent system of the trigeminal nerve reached similar conclusions, viz., that deep pain sensations from the muscles of the face are carried by the facial nerve. Needle electrodes were inserted in the deep structures of the face, and painful reflexes were elicited after the trigeminal nerve had been completely severed. After section of the facial nerve on the same side these pain reflexes were obliterated, which shows that the facial nerve contains afferent fibers.

There are also a number of experiments which showed the relationship of this afferent system to the cells of the geniculate ganglion. Van Gehuchten,[25] after cutting the facial nerve in rabbits as it emerged from the facial canal, observed that the majority of the cells of the geniculate ganglia were normal. In every instance, however, a small number of cells showed evidences of chromatolysis, which indicates the existence of sensory fibers in the trunk of the facial nerve. Amabolino [26] in the same year, in experiments on dogs, found that section of the chorda tympani nerve in the middle ear caused degeneration of about four fifths of the cells of the geniculate ganglion. The facial nerve on the opposite side was cut at its exit from the stylomastoid foramen, with no resulting degeneration of the cells of the geniculate ganglion. In these experimental studies, as van Gehuchten pointed out, Amabolino probably overlooked the few cells which degenerate after section of the facial nerve at the stylomastoid foramen.

De Gaetano [27] carried out similar experiments on dogs, rabbits and guinea-pigs. He observed that section of the chorda tympani nerve was accompanied by retrograde degeneration in from three fourths to four fifths of the cells of the geniculate ganglion. Section of the seventh nerve at its exit from the facial canal caused degeneration of most of the other cells. The few remaining cells which were not degenerated were referred to the great superficial petrosal nerve.

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24. Gerard, M. W.: Afferent Impulses of the Trigeminal Nerve: The Intramedullary Course of the Painful, Thermal and Tactile Impulses, Arch. Neurol. & Psychiat. **9**:306 (March) 1923.

25. van Gehuchten, P.: Recherches sur l'origine réele des nerfs craniens, J. de neurol. et hypnol. **3**:302, 1898.

26. Amabolino: Sur rapporte del ganglio geniculato con la corda del timpano ecol faciale, Pisani **19**:2, 1898; abstr., Jahrb. u. d. Fortschr. d. Neurol. **2**:219, 1898.

27. de Gaetano, L.: Del nervo intermediario di Wrisberg, Neuraxe **8**:67, 1906; abstr., Zentralbl. f. norm. u. path. Anat. **4**:184, 1907.

Davis also cut the facial nerve at the exit from the stylomastoid foramen in a series of cats. Histologic examination of the geniculate ganglion showed chromatolysis of some of the ganglion cells, thus corroborating the earlier observations of van Gehuchten and de Gaetano.

The relation of the great superficial petrosal nerve to the cells of the geniculate ganglion was also confirmed by Zagita [28] in dogs. This observer noted that after section of the great superficial petrosal nerve there followed retrograde degeneration of about one twelfth of the cells of the geniculate ganglion which are distributed in the tip of the geniculate ganglion, where this nerve takes its origin.

A point should be considered in interpreting these experimental studies on the relation of the deep sensory portion of the facial nerve to the cells of the geniculate ganglion: It is known that the cutaneous branches of the facial nerve leave the trunk just as it emerges from the stylomastoid foramen. It would therefore be easy to injure them in experimental sections of the trunk at this level, which would of course cause retrograde degeneration of the geniculate cells related to the somatic sensory component.

These various experiments on animals show that the chorda tympani nerve, the great superficial petrosal nerve and the facial nerve proper all contain sensory fibers which originate in the geniculate ganglion.

One may assume on the basis of these experimental studies that similar conditions exist in the geniculate system in man. In man, however, because of the greater development of the facial musculature and its functional importance, the numerical relationship of the nerves to the cells of the geniculate ganglion may not be the same as in lower animals.

The observations of His Jr.[29] made many years ago on the geniculate ganglion of a 22 mm. human embryo throw some light on this question. This investigator determined by actual count that the chorda tympani nerve contains about 120 fibers, while the number of cells of the geniculate ganglion ranges from 7 to 800. This indicates that the geniculate ganglion in man contains a sufficient number of cells to account for all its sensory functions which are known today, viz., the gustatory, the cutaneous, the intra-oral and those of deep sensibility. This is all the more true as it is known that additional ganglion cells of similar type are observed along the nerve trunks near the geniculate ganglion.

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28. Zagita: Einige Experimente an dem Nervus petrosus superficialis major zur Bestimmung des Ursprungsgebietes des Nerven, Folia neuro-biol. **8**:361, 1914.

29. His, W., Jr.: Zur Entwicklungsgeschichte des Acoustico-Facialis Gebietes beim Menschen, Arch. f. Anat. u. Physiol., supp., 1889, p. 1.

Weigner,[30] in a careful study of the nerve of Wrisberg in man, demonstrated the existence of many ganglion cells of the same type as those observed in the geniculate ganglion scattered along the course of the nerve of Wrisberg, the great superficial petrosal nerve, the chorda tympani nerve and the trunk of the facial nerve, near the ganglion. These he regarded as microscopic accessory ganglia belonging to the geniculate system, which considerably augment the range of its function.

It appears from these observations that the cells of the geniculate system are by no means limited to the geniculate ganglion but are scattered along the various branches of the adjacent nerve trunks. This should be considered in future experiments when an attempt is made to localize the cells of origin by the method of retrograde degeneration.

It is of interest in comparison to note the ganglionic relations of the fibers of deep sensibility in the trigeminal nerve. In this nerve conditions are quite different. Fibers for deep sensibility supplying the muscles of mastication are carried by the motor root of the fifth nerve directly to a central structure in the pons—the nucleus mesencephalicus trigemini—which is the ganglionic representation of deep sensibility in the trigeminal nerve.

Willems [31] recently investigated this problem in rabbits and showed that the motor branch of the trigeminus nerve, supplying the muscles of mastication, has its central ganglionic representation of deep sensibility in the nucleus mesencephalicus trigemini.

The descending mesencephalic root of the fifth nerve and its relation to deep sensibility were also demonstrated by Allen [32] in the guinea-pig. This centrally situated nucleus is therefore the homolog of the spinal ganglion in the fifth nerve.

There is, however, no reason in the present state of knowledge to refer the deep sensory innervation of the facial nerve to a central structure, such as exists in the trigeminal nerve. This anatomic fact is important in its relation to the character and distribution of pressure pain in cases of geniculate neuralgia.

There is definite clinical and experimental evidence that the facial nerve supplies the region of the face with deep sensibility, i. e., sensation of tactile and painful pressure, localization of deep touch and sense of position. The afferent fibers of deep sensation are conveyed by the facial nerve to the cells of the geniculate ganglion and the

30. Weigner, K.: Ueber den Verlauf des Nervus intermedius, Anat. Hefte **29**:99, 1905.

31. Willems, E.: Les noyaux masticateur et mésencéphalique du trijumeau chez la lapin, Neuraxe **12**:175, 1911.

32. Allen, W. F.: Radix Mesencephalica Trigemini in the Guinea Pig, J. Comp. Neurol. **30**:169, 1918.

accessory geniculate cells of the trunk and the nervus intermedius. This viscerosensory system of deep sensibility must therefore be considered in the neuralgic syndrome of the nervus facialis.

GENICULATE NEURALGIA (NEURALGIA FACIALIS VERA)

In my original study of neuralgia of the seventh cranial nerve, primary, secondary and reflex forms were described. The more exact anatomic knowledge now available gives a clearer idea of the extent and distribution of the pain in geniculate neuralgia than was possible

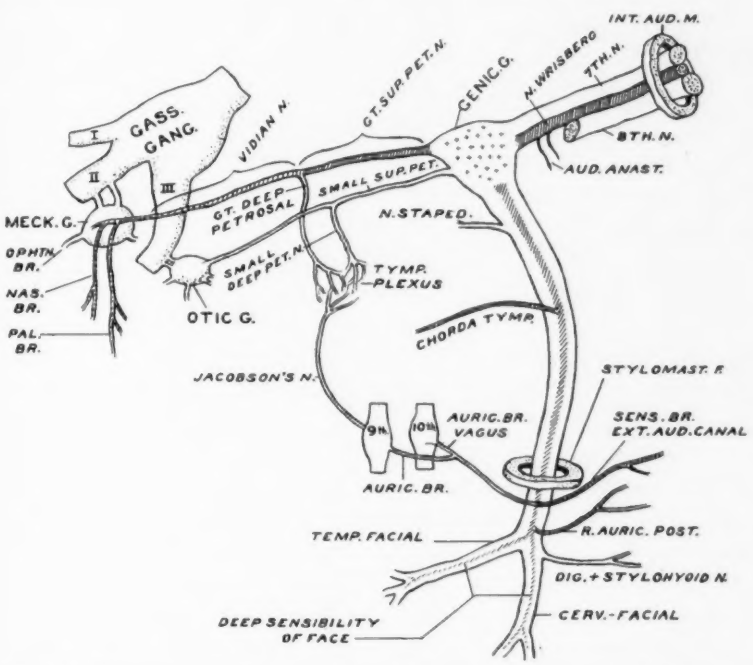

Fig. 7.—Diagrammatic representation of the facial nerve, showing the geniculate ganglion and its sensory root and peripheral divisions (Hunt). The sensory system is shaded.

at the time of my original study. As was indicated in the section on the anatomic features, the sensory system of the facial nerve has four separate pathways for the transmission of sensory impulses, three of which play an important rôle in the distribution of pain in neuralgia of the facial nerve (fig. 7):

1. Sensory filaments passing from the geniculate ganglion through the trunk of the facial nerve to the tympanum and the cutaneous area

on the external ear (zoster zone of the geniculate system) and the connections between the geniculate system and the terminations of the auditory nerve in the internal ear.

2. Sensory fibers of the great superficial petrosal and the vidian nerve passing from the geniculate ganglion through the sphenopalatine ganglion, where they are in relation with its orbital, posterior nasal and palatal branches.

3. Fibers of deep sensibility of the face, which originate in the cells of the geniculate ganglion and pass with the peripheral motor branches of the nerve to the facial musculature.

4. The chorda tympani nerve, which conveys fibers for taste and a vestigial remnant of fibers for common sensation to the anterior two thirds of the tongue. (This branch is essentially gustatory.)

These various pathways bring the geniculate system into direct relation with the internal and the external ear, the muscles and tendinous structures of the face and the posterior orbitonasopalatal regions. The pain of geniculate neuralgia therefore follows this distribution.

In a consideration of the clinical aspects of neuralgia the known anatomic distribution is of first importance, for neuralgia, while originally a painful condition of a single nerve or filament, tends gradually to diffuse itself in the distribution of the whole ganglionic system. Accordingly, in a case of complete geniculate neuralgia one would expect pain in the ear (otalgia) and in the deeper structures of the face and posterior orbitonasopalatal regions (deep prosopalgia).

Partial forms of neuralgia are well known and are common in cases of trigeminal neuralgia, in which pain in a single division may precede by months and years extension to the whole ganglionic system.

The same tendency is also evident in the other mixed cranial nerves —the facial, the glossopharyngeal and the vagus nerve.

In cases of severe neuralgia the pain may radiate and even pass beyond the boundaries of the affected ganglionic distribution into other areas; whether this takes place by reason of peripheral anastomoses with neighboring systems or through central connections in the sensory nuclei of the brain stem is not known. These peculiarities, however, should all be considered when one attempts to outline and interpret the distribution of pain in an obscure system, such as the geniculate.

GENICULATE NEURALGIA (POSTHERPETIC FORM)

In geniculate neuralgia primary, secondary and reflex forms are recognized. Of the secondary forms, the most common is that following herpetic inflammation of the geniculate ganglion. An important

symptom of geniculate herpes zoster is severe otalgia. This pain is localized chiefly in the depths of the ear and on certain areas of the external ear, within the geniculate zoster zone. It is often lancinating and very severe and extends into the mastoid and occipital regions and into the face. In severe forms pain is felt in the neck and shoulder of the affected side. The severity of the local pain sometimes simulates that of mastoiditis, and in some cases operation has been performed to relieve a supposed infection of the mastoid. As a rule, the severe pain lasts only a few days or a few weeks and then gradually subsides. In rare cases it persists longer.

The patient in the following case, who came under my observation in 1916, presented neuralgic pains of geniculate distribution three years after an attack of herpes zoster oticus:

A physician, after a severe "cold" associated with pharyngitis, was seized with violent pains in the ear. This was soon followed by the development of a herpetic eruption in the external auditory canal and the external meatus, which became swollen and partially closed. The tympanum was free from vesicles. About the same time palsy of the facial nerve developed, and the sense of taste was lost over the anterior two thirds of the tongue on the affected side. The auditory nerve was not involved.

In the course of a few weeks the palsy practically disappeared; taste returned, and the vesicles healed, leaving a few minute scars. The pains in the ear were lancinating and severe for six weeks, when they gradually diminished in severity. Ever since the attack, three years before, there had persisted an aching pain in the ear, which was also present in the face, especially over the cheek, the temple and the postorbital region. The pain was increased by fatigue and exposure to cold.

Examination revealed slight residual signs of former paralysis of the facial nerve, viz., slight associated movements of the chin muscles on the affected side on closure of the eyes; otherwise, movements were good in all three branches of the nerve. Of interest was the persistence of a slight ticlike movement in the upper portion of the platysma muscle.

The patient consulted me for relief of the persistent neuralgia, which was felt in the depth of the ear, the mastoid and the neighboring occipital region and which radiated deeply into the face. This pain was no longer lancinating, but of a dull aching character. The whole side of the face and ear were sensitive to cold in winter, and the patient turned up the flap of his coat for protection.

This case was a typical instance of herpetic inflammation of the geniculate ganglion, with involvement of the chorda tympani and the facial nerve. It is of interest because of the severe and persistent type of postherpetic neuralgia, which involved not only the ear (otalgia) but the deeper structures of the face (deep prosopalgia).

The existence of deep neuralgia of the face in this case is of especial interest because of its bearing on the nature and distribution of the pain in cases of complete geniculate neuralgia.

GENICULATE NEURALGIA (OTALGIC FORM)

In my paper,[2a] published in 1907, special emphasis was placed on the otalgic nature of the pain. My conclusions were summarized as follows:

> At the present time we have not a clear . . . conception of that peculiar localization of neuralgia termed otalgia. Because of the complexity and overlapping of the auditory innervation, certain mixed forms of otalgia must occur. These belong rather to the auriculo-temporal neuralgia of the trigeminus, or are occipito-cervical otalgias; not, however, otalgia in the pure sense of this term. The pure and more sharply localized form of otalgia is, I believe, essentially a manifestation of the sensory system of the facial nerve.
>
> It may be said that the glosso-pharyngeal nerve, which sends a tympanic branch to the tympanic plexus, may also be one of the underlying factors in otalgia. In answer, I would mention the other sensory branches of the 9th nerve: to the tonsil, to the palatal arch and pharynx, and the fact that this area is not involved in the pure forms of otalgia. Of course, I cannot deny that the sensory system of the glosso-pharyngeal nerve may be the seat of a neuralgic affection, either alone or in conjunction with that of the facial. In such an event, however, one would naturally look for the distribution of pain in the throat as well, and not in the ear alone. The vagus, on the other hand, has only a small cutaneous representation on the auricle, and could therefore hardly be brought within the realm of otalgia except in a secondary or subordinate sense.

Since this statement was made, glossopharyngeal neuralgia has been recognized, and numerous cases have been reported in which surgical intervention was successful.

I shall now cite two cases, one of facial and the other of glossopharyngeal origin, which because of the light they throw on otalgia are especially important.

Clark and Taylor [33] reported their historic case of tic douloureux of the sensory filaments of the geniculate ganglion, with operation and recovery, in 1910.[33b] The pains were typically neuralgic—paroxysmal, lancinating and severe—and of two years' duration. They were localized chiefly in the depth of the ear, the anterior wall of the external meatus and a small area just in front of the ear and were associated with redness of the external auditory canal. At times there was a moderate degree of neuralgic pain in all three distributions of the trifacial nerve and in the occipital region. The case was studied by a number of neurologists, and all agreed on the typical neuralgic character of the pain and its relation to the geniculate area which I had described. The pain was relieved by intracranial section of the seventh nerve, which included the posterior root, or the pars intermedia of Wrisberg. The patient was under observation for some time after operation, and six years after section of the root she reported complete freedom

33. Clark, L. Pierce, and Taylor, A. S.: (*a*) True Tic Douloureux of the Sensory Filaments of the Facial Nerve, J. A. M. A. **53**:2144 (Dec. 25) 1909; (*b*) Tic Douloureux of the Sensory Filaments of the Geniculate Ganglion: Operation, Recovery, J. Nerv. & Ment. Dis. **37**:242, 1910; (*c*) Echter Tic Douloureux der sensiblen Fasern des N. Facialis: Operation und Heilung, Neurol. Centralbl. **30**: 1154, 1911.

from neuralgic pain. One would therefore seem justified in accepting a case of this kind as confirmation of my views on the sensory system of the seventh nerve and its relation to neuraliga.

Reichert, among others,[34] reported a case of tympanic plexus neuralgia in which cure was effected by intracranial section of the glossopharyngeal nerve. A woman aged 31, a telephone operator, after an attack of coryza in August 1932, was seized with a sharp, stabbing pain deep in the left external auditory canal. The attacks of pain were paroxysmal and severe. In addition there were aching pains in the left side of the face and nose, the left eyeball and the left parieto-occipital area. There was sensitiveness over the mastoid and the pretragal regions and in the external auditory canal. There were injection and swelling of the postero-superior wall of the external auditory meatus.

The case was regarded as an instance of geniculate neuralgia, similar to that reported by Clark and Taylor, and an operation was performed with the use of local anesthesia to facilitate localization of the sensory filaments of the facial nerve.

On Dec. 10, 1933, with the use of the unilateral approach of Dandy, the seventh, eighth, ninth and tenth nerves on the left were exposed and identified. When the bundle of the seventh and eighth nerve fibers was gently touched and moved, the patient felt pain in the auditory canal, but it was not the pain characteristic of tic. The ninth nerve was then touched, and the ticlike pain was immediately induced. The glossopharyngeal nerve was then cut, with complete relief of pain, which had not returned after four months.

Reichert concluded his study with the statement: "The patient had a tic douloureux of the tympanic branch of the glossopharyngeus (Jacobson's nerve or plexus), and since her symptoms were identical with those of the patient of Clark and Taylor, their case undoubtedly was likewise a Jacobson's nerve neuralgia." He stated further that two types of glossopharyngeal neuralgia should be recognized: a complete form, which is that usually encountered, and a partial form, which is limited to Jacobson's branch of the ninth nerve, or tympanic plexus neuralgia.

It is clear from Reichert's complete study and brilliant operative results that the case was an instance of tympanic plexus neuralgia involving the tympanic branch of the glossopharyngeal nerve. His other conclusion, that the geniculate neuralgia in the case of Clark and Taylor was also of glossopharnygeal origin, is not justified. The relief of pain in the case of geniculate neuralgia followed immediately section of the root of the seventh nerve. It had not recurred after an interval of six years. This should be considered proof of its geniculate origin, by the same reasoning that justified Reichert in ascribing tympanic plexus neuralgia in his case to the glossopharyngeal nerve.

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34. Reichert, F. L.: Tympanic Plexus Neuralgia: True Tic Douloureux of the Ear or So-Called Geniculate Neuralgia; Cure Effected by Intracranial Section of the Glossopharyngeal Nerve, J. A. M. A. **100**:1744 (June 3) 1933. Erickson, T. C.: Paroxysmal Neuralgia of the Tympanic Branch of the Glossopharyngeal Nerve, Arch. Neurol. & Psychiat. **35**:1070 (May) 1936. Lillie, H. I., and Craig, W. M.: Anomalous Vascular Lesions in Cerebellopontile Angle: Severe Neuralgic Pain in the Ear and Profound Nervous Disturbance; Operation and Recovery, Arch. Otolaryng. **23**:642 (June) 1936.

Furthermore, the relation of the sensory system of the geniculate ganglion to the auditory mechanism and the external ear is now well established and has been recognized by such leading authorities as Testut and Latarjet,[9] Déjerine [35] and Roger and Binet; [36] when one considers that separate sensory filaments of the facial nerve pass directly to the external ear, there is no reason why partial neuralgia (otalgia) may not occur in this distribution as well as in that of the glossopharyngeal nerve. It is now known that the cutaneous filaments of the facial nerve to the tympanum and the auricle leave the trunk immediately after its exit from the stylomastoid canal, where they are vulnerable to pressure and the effects of refrigeration.

The geniculate and glossopharyngeal ganglia are both concerned in the innervation of the auditory mechanism, and apparently either nerve may be the seat of otalgia which does not involve to any marked degree the whole sensory distribution of the affected nerve.

Dandy,[37] in an analysis of twenty cases of glossopharyngeal neuralgia, recorded three cases, two of which were reported by Doyle and one by Adson, in which the original pain was at first localized in the ear, only later appearing in the classic distribution of the glossopharyngeal nerve. In nearly all other cases there was associated pain in some portion of the auricular region—the meatus, the concha, the lobule or in front of or behind the ear. This is additional evidence of the existence of partial glossopharyngeal neuralgia (otalgia).

Therefore, in the geniculate, glossopharyngeal and trigeminal fields partial forms of neuralgia may appear, in which the pain is chiefly localized, viz., in one or another of the sensory branches, as well as the complete form, in which the whole system is the seat of severe neuralgic pain. Even in cases of neuralgia of the superior laryngeal nerve of vagal origin, associated otalgia involving the auricular branch of the vagus nerve is not always present.

Later investigations of this subject, both clinical and anatomic, show that in the majority of cases geniculate neuralgia has a wider distribution of pain than was at first assumed. It is not merely otalgia with radiations into the face and mastoid, but it includes deep facial neuralgia involving the other sensory divisions of the geniculate system, viz., the great superficial petrosal nerve and the deep sensory system of the seventh nerve. The anatomic evidence bearing on this question has already been given, and now I shall give clinical data in support of this view.

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35. Déjerine, J.: Ganglion geniculé de facial sémeiologie du système nerveux, Paris, Masson & Cie, 1914, p. 834.

36. Roger and Binet: Le syndrome geniculé, in Roger, G.-E.-H.: Traité de physiologie normale et pathologique, Paris, Masson & Cie, 1936, vol. 10, p. 427.

37. Dandy, W.: Glossopharyngeal Neuralgia (Tic Douloureux): Its Diagnosis and Treatment, Arch. Surg. **15**:198 (Aug.) 1927.

GENICULATE NEURALGIA (PROSOPALGIC FORM)

The more definite knowledge of the extent and distribution of the sensory system of the geniculate ganglion now available clarifies much that was previously obscure in the domain of its neuralgic affections. Today one must consider not only otalgia with its radiations but a deep form of prosopalgia as an integral part of the geniculate neuralgic syndrome.

These cases of deep prosopalgia are, I believe, scattered in various groups of painful disorders of the face, which are described under such headings as atypical neuralgia of the face, sphenopalatine and vidian neuralgia and sympathalgia and perhaps also a type referred to by Cushing as painful *tic convulsif*. I do not mean that in any considerable number of cases of these conditions the neuralgia is solely of geniculate origin but merely that cases of geniculate neuralgia are to be found within these groups. When one is armed with this knowledge, it should be possible in the future to recognize deep facial neuralgia of the geniculate group as well as geniculate otalgia.

Atypical Facial Neuralgia.—For many years, as knowledge of trigeminal neuralgia increased, it has become apparent that there is another large group of cases in which the condition resembles but is not true trifacial neuralgia. The best proof of this is persistence of the disorder after successful surgical procedure on the gasserian ganglion. This condition is now termed atypical facial neuralgia and has received careful study by observers who are interested in trigeminal neuralgia and its surgical treatment.

The cases have been variously interpreted, and it is probable that several types are represented within the larger group. In some instances the possibility of central pain has been suggested, which would not be modified by procedures on the peripheral ganglion or its divisions. In other cases the pain has been referred to the sympathetic system, and already a considerable literature deals with this phase of the subject. Other cases are to be found in a large, complex group in which the condition is known as Sluder's syndrome. A psychogenic etiology has also been suggested, and many cases are classified as instances of hysteria, psychalgia or hypochondriasis, but methods of treatment which are usually successful in cases of the psychogenic form are without avail in those of the atypical type. All observers recognize the obscure nature of the clinical picture and the unsatisfactory results obtained with surgical treatment.

In a critical study of one hundred and forty-three cases of atypical neuralgia Glaser [38] made a careful analysis of the symptomatology. As

38. Glaser, M. A.: Atypical Neuralgia, So Called: A Critical Analysis of One Hundred and Forty-Three Cases, Arch. Neurol. & Psychiat. **20**:537 (Sept.) 1928.

to one outstanding characteristic all observers concur: The pain is not superficial; it is not referred to the surface as is that of true trigeminal neuralgia, but is deep seated in the tissues, the bone and the eyeball. The pain does not follow the direction of the several divisions or branches of the trigeminal nerve but jumps across anatomic boundaries and extends often beyond the trigeminal zone into the neck and the arm.

The pains of trigeminal tic douloureux are characterized by thermal sensations and sharp, cutting, stabbing pain and those of atypical neuralgia by pressure sensations, such as throbbing, gripping, pulling and bursting. Glaser said:

> One is led to speculate as to the significance of these conspicuous distinctions, and at once the question of what part the facial nerve, to which is attributed the sense of pressure, may play.

The pain of tic douloureux is essentially paroxysmal, with intervals of complete relief, and that of atypical neuralgia is essentially persistent and continuous, with periods of days in which there are severe exacerbations. During the first two or three hours of these periods of aggravation, the pain gradually increases until the height of severity is reached, after which the intensity slowly subsides, until at the end of the third day or so the chronic phase is resumed.

In Glaser's series, in addition to pain, many patients had associated sympathetic phenomena. Of the entire series of one hundred and forty-three patients, sixty-five had pain alone and seventy-six associated sympathetic phenomena. The frequent association of sympathetic phenomena and pain suggested the sympathetic system as the origin of the pain in atypical neuralgia.

Frazier and Russell [39] also reviewed a series of sixty cases of atypical facial neuralgia. The following differences were noted in contrasting typical trigeminal neuralgia with the atypical forms:

> . . . The [distribution of the] pain is not referred to the peripheral distribution of the nerve; that is, not to the lips, chin, ala of the nose; rather to the cheek, temple, orbit, in front or behind the ear, occasionally to the jaws. . . . The pain does not radiate along the course of one or the other nerve tract. It seems unrelated to any anatomic distribution. It will jump across from one zone of the three divisions to another, but never to the periphery. . . . The pain extends beyond the trigeminal territory; behind the ear, to the submaxillary region, to the shoulder and arm.
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> . . . In the majority of cases the character of the pain is described as drawing or pulling. The thought of a pressure disturbance seems dominant; the tissue of

39. Frazier, C. H., and Russell, E. C.: Neuralgia of the Face: An Analysis of Seven Hundred and Fifty-Four Cases with Relation to Pain and Other Sensory Phenomena Before and After Operation, Arch. Neurol. & Psychiat. **11**:557 (May) 1924.

the region feels as though under tension; or the pain may be described as burning, an ache, sometimes boring or throbbing, rather than cutting, stabbing or tearing. It is almost always deep seated, deep in the orbit, deep in the cheek or temple, not superficial or terminal and what is particularly noteworthy, it is constant and not intermittent or paroxysmal, though varying in its intensity.

They further stated that:

. . . In reviewing the atypical cases we have kept in mind the sphenopalatine ganglion as a possible factor, but we have been unable to recognize any syndrome which would justify the recognition of such a distinct clinical entity. In fact, it is difficult to find enough similarity in the atypical neuralgias to justify any classification. The diversity of the clinical picture is one of the outstanding peculiarities. In only the exceptional case did cocainization of the sphenopalatine ganglion have any influence on the pain. In one case, in which a provisional diagnosis of sphenopalatine neuralgia was made, the removal of the sphenopalatine ganglion did not give entire relief.

Relation of Atypical Neuralgia to the Sympathetic System (Sympathalgia).—In addition to the fifth and the seventh nerve, the sympathetic nervous system has also been under suspicion as an etiologic factor of importance in this form of neuralgia. The French writers Alajouanine and Thurel[40] spoke of it as *sympathalgies faciales,* the symptomatology of which does not differ essentially from so-called atypical neuralgia and the sphenopalatine neuralgia of Sluder.

Frazier,[41] in ten cases of atypical neuralgia, attempted to relieve the condition by operation on the cervical portion of the sympathetic system. Of this number one patient alone obtained relief, but the course could not be followed. Frazier stated that the operation not only did not afford relief but exaggerated the condition in some patients.

Peet[42] also investigated the rôle of the sympathetic nervous system. He stated:

The term atypical neuralgia is unsatisfactory for two reasons: the pains are not neuralgic in character, and a number of unrelated conditions are probably grouped under the one designation.

Unless of central origin, pain referred to the face must involve the trigeminal, the facial or the sympathetic nerves.

The peripheral trigeminal tract has been eliminated from consideration by the persistence of atypical neuralgic pain after section of the sensory root of the gasserian ganglion.

One type of so-called atypical neuralgia should be considered of central origin, the lesion being probably located in the trigeminal tract in the medulla or the pons.

40. Alajouanine, T., and Thurel, R.: Les sympathalgies faciales, J. méd. franç. **22**:188 (June) 1933.

41. Frazier, C. H.: Atypical Neuralgia: Unsuccessful Attempts to Relieve Patients by Operations on the Cervical Sympathetic System, Arch. Neurol. & Psychiat. **19**:650 (April) 1928.

42. Peet, M. M.: The Rôle of the Sympathetic Nervous System in Painful Diseases of the Face, Arch. Neurol. & Psychiat. **22**:313 (Aug.) 1929.

Sensory fibers from various nerves, especially the vagus, may be incorporated in certain sympathetic nerves, although proof of such association is lacking. If found they will furnish an explanation for the transmission of painful sensations from the blood vessels. Only in this gross anatomic sense can the sympathetic system be considered sensory.

Atypical neuralgic pain can be of sympathetic origin only if such pain is due to vasomotor spasm, since this system carries only afferent impulses.

Fay,[43] one of the most enthusiastic of investigators espousing a sympathetic etiology, spoke of atypical facial neuralgia as "a syndrome of vascular pain." He expressed the belief that the pain follows the course of the vascular tree. In one case of atypical neuralgia seven operations were performed for relief of pain: (1) section of the trigeminal root; (2) resection of the sphenopalatine ganglion and the upper branches of the seventh nerve; (3) ablation of the cervical portion of the sympathetic trunk below the superior cervical ganglion; (4) stripping of the common carotid artery; (5) section of the hypoglossal nerve; (6) extracranial section of the glossopharyngeal nerve, and (7) section of the sensory branches of the vagus nerve, the jugular branch of the vagus nerve and Arnold's nerve and division of the sheath of the vagus and of vagus fibers to the internal and the external carotid artery. Division of the sheath of the vagus nerve produced marked relief of the neuralgia and disappearance of carotodynia, which he regarded as an important symptom.

In a similar case, section of the trigeminal root was performed, and subsequently ablation of the cervical portion of the sympathetic trunk, extracranial section of the sensory division of the vagus nerve, the glossopharyngeal nerve and Arnold's nerves, avulsion of the occipitalis major nerve, stripping of the common carotid artery below the bifurcation and section of the superficial cervical plexus were carried out. The patient had some relief of pain after each operation, but although the condition was improved, he still had a great deal of pain in the malar region and the eye. It is evident from the description that there exist atypical forms of neuralgia of such severity as to justify multiple operations, in an attempt to relieve pain. Operative procedures on the trigeminus and sympathetic nerves and other mixed cranial nerves, exclusive of the facial nerve, were not effective in producing complete relief. The question arises whether the geniculate system may not be involved in such cases.

Fay concluded from his study that superficial pain is conveyed by way of the trigeminus nerve and cervical branches and that deep pain sense is transmitted through the sensory branches and the connections of the vagus nerve.

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43. Fay, Temple: Atypical Facial Neuralgia: A Syndrome of Vascular Pain, Ann. Otol., Rhin. & Laryng. **41**:1030, 1932.

Sphenopalatine Neuralgia.—Sphenopalatine ganglion neurosis, or lower half headache (Sluder's Syndrome),[44] is represented by another large and complex group of cases which should be carefully scanned for geniculate neuralgia, more especially as the geniculate ganglion stands in close relation to the sphenopalatine ganglion and its orbital, nasal and palatal branches through the great superficial petrosal and vidian nerves.

This form of neuralgia was first described by Sluder in 1908, and the original report was elaborated in many additional articles, which are summarized in his book, entitled "Nasal Neurology."

According to Sluder, the pain of sphenopalatine neuralgia has a wide distribution and is localized in the root of the nose, in and about the eye and in the upper part of the face and the upper teeth and sometimes also in the lower jaw, the lower teeth, in the temple and about the zygoma, the ear, the mastoid, the occiput and the neck. It may extend to the shoulder and less often to the axilla and the breast, and in severe attacks, to the arm, the forearm, the hand and even the finger-tips.

In addition to this neuralgic syndrome, vasomotor and secretory symptoms referable to the sympathetic system are also described. Among the sympathetic manifestations are severe and protracted sneezing, marked congestion of the mucous membrane, with abundant secretion of the nasal mucosa (hydrorrhea), and nasal asthma. He stated that these symptoms are sometimes the only indication of involvement of the sphenopalatine ganglion. The sympathetic syndrome occurs less frequently than the neuralgic type, but usually they are combined.

Sluder obtained relief in many cases by injection into the sphenopalatine ganglion. He emphasized the relation of the middle branch of the trigeminus nerve, the vidian branch of the geniculate ganglion and the sympathetic system to the syndrome and the proximity of all these structures of the sphenomaxillary fossa to the sphenoid and posterior ethmoid cells, with the consequent dangers of infection.

While the dependence of this syndrome on the sphenomaxillary ganglion has been questioned by many, the relation of its multiform symptomatology to the important neural structures of the sphenomaxillary fossa cannot be denied.

Of especial importance to this question is the close relation of the vidian nerve to the nasal ganglion and the other structures of the sphenomaxillary fossa. This relationship was recognized by Sluder, who described vidian neuralgia and even subjected the vidian nerve to

44. Sluder, Greenfield: Nasal Neurology, St. Louis, C. V. Mosby Company, 1927, p. 93. A complete bibliography is included.

electrical stimulation in the pterygomaxillary fossa, producing pain which was referred to the ear, mastoid, neck, shoulder, arm and forearm.

Vail [45] also directed attention to this problem, and emphasized the close relationship of the great superficial petrosal nerve to the apex of the petrous pyramid; he referred the typical ocular pain of inflammation of the cells of the petrous pyramid to this nerve and its continuation in the vidian nerve.

He further stated [46] that vidian neuralgia is characterized by pain in the nose, face, eye and ear and sometimes the neck and shoulder and that it may or may not be associated with symptoms of nasal sinusitis. He expressed the belief that sphenopalatine neuralgia is really vidian neuralgia.

This whole question was made the subject of careful analysis by Ruskin,[47] who concluded that the sphenopalatine ganglion syndrome of Sluder is not a distinct clinical entity but is composed of four distinct syndromes: maxillary, sensory facial, sympathetic and local sphenopalatine (cells of the ganglion proper). In any given case these syndromes are usually present in various combinations.

Painful Tic Convulsif.—Another rare group of neuralgias which must be considered in the quest for geniculate neuralgia was described several years ago by Cushing [48] as painful *tic convulsif*. He had seen three cases. The condition is characterized by severe pain in the trigeminal region, associated with marked spasm of the facial muscles.

In the first case, a man aged 52 gave a history of severe neuralgia for forty-two years. It originated in the ophthalmic division; two years later it extended to the maxillary nerve and later involved the whole trigeminal field. From the onset the condition had been characterized by marked motor spasms, which seemed to inaugurate the paroxysms. The original pain was referred to the eyeball. A surgeon had removed the eye in 1897. In the following year supra-orbital neurectomy was performed. In 1904 all the teeth were extracted. Two ineffectual attempts had been made to remove the ganglion by the Hartley-Krause method.

On June 18, 1909, Cushing removed the remains of the ganglion and its sensory root, leaving total anesthesia in the trigeminal area. The spasms and pain continued unabated. On July 12 the right facial nerve was exposed in the fallopian canal; an effort was made to destroy the geniculate ganglion, and a

45. Vail, Harris H.: Syndrome of Pain in Reference to the Ear, Eye, Nose and Throat, Tr. Am. Acad. Ophth. **38**:255, 1933. Vidian Neuralgia, with Special Reference to the Eye and Orbital Pain in Suppuration of the Petrous Apex, Arch. Otolaryng. **17**:212 (Feb.) 1933.

46. Vail, Harris H.: Vidian Neuralgia, Ann. Otol., Rhin. & Laryng. **41**:837, 1932.

47. Ruskin, S. L.: Contribution to the Study of the Sphenopalatine Ganglion, Laryngoscope **35**:87, 1925.

48. Cushing, Harvey: The Varieties of Facial Neuralgia, Am. J. M. Sc. **157**: 160, 1920.

spinofacial anastomosis was then made. This was followed by disappearance of the tic and the first moderate relief the patient had had for two years, though it was not complete, for he still complained of pain in the face. After an interval of six months, the spasms returned over the spinofacial route. The pain gradually extended into the ear and became so insufferable that further oral operations were undertaken at his home, where he died after an operation on Oct. 28, 1913. According to a postmortem report there had been complete removal of the right trigeminal nerve.

In two other cases similar successful operations on the trigeminal nerve failed to relieve the pain.

Cushing also cited another case, that of a colleague, in which the pain and associated motor spasm were permanetly cured by spinofacial anastomosis. "These curious cases," he stated, "may possibly be attributable to a lesion of the geniculate ganglion as suggested by Hunt."

COMMENT

There is anatomic and clinical evidence that geniculate neuralgia may appear both as otalgia and as deep prosopalgia.

In the complete form there are both otalgia and deep prosopalgia, with associated pain in the distribution of the cervical nerves.

In geniculate otalgia the chief pain is localized in the depths of the ear and the auricle, with radiation into the face and the occipital region.

In geniculate prosopalgia the pain is referred to the deeper structures of the face, the orbit and the posterior nasal and the palatal region. In severe types the pain radiates to the ear, the occipital region, the neck and the shoulder. There are grounds for the assumption that the painful pressure sensations which are present in atypical neuralgia are also of geniculate origin.

When one considers the great frequency of trigeminal neuralgia and the comparative frequency of glossopharyngeal and even of superior laryngeal (vagal) neuralgia, one should not expect an important sensory system like that of the geniculate to escape.

I believe that cases of geniculate neuralgia occur but are concealed in the large clinical groups already mentioned.

It is only too well known what a variety of conditions are included in the large group of atypical neuralgias and that the results of treatment are unsatisfactory. In any future study of this question neuralgia of the seventh cranial nerve should be carefully considered.

CONCLUSIONS

In the foregoing sections I have described the sensory distribution of the facial nerve and its relation to neuralgia in the light of advances which have been made in the past twenty-five years. Since my earlier publications, anatomic and clinical evidence has accumulated which

confirms the opinion I expressed at that time that the facial nerve is a mixed nerve, with a somatic and a visceral sensory system and a corresponding neuralgic syndrome.

I have also presented a summary of my earlier views on this subject and the modifications which they have undergone, with increasing knowledge and experience.

At present the geniculate system is known to have (fig. 7): 1. Sensory filaments to the internal ear and branches to the zoster zone of the auricle, which bring it into close relation with the auditory mechanism. These branches are responsible for the otalgia.

2. The sensory system of the great superficial petrosal nerve, which brings the geniculate ganglion into close relation with the orbital, nasal and palatal branches of the sphenopalatine ganglion and the maxillary division of the fifth nerve. These branches are responsible for the deep prosopalgia.

3. A viscerosensory system subserving deep sensibility of the face, which is the seat of painful pressure sensations in geniculate prosopalgia.

These various branches of the sensory facial system have numerous anastomotic connections with the trigeminal, glossopharyngeal and vagal systems, as well as with the branches of the cervical plexus.

Not only are there these superficial connections, but the central sensory nucleus of the facial nerve stands in close anatomic relationship with those of the other mixed cranial nerves.

The central and peripheral associations with neighboring sensory systems account for the wide diffusion of pain in severe geniculate neuralgia.

It should be added that the facial nerve is especially rich in sympathetic and parasympathetic fibers, which explain the associated vasomotor and secretory manifestations.

Neuralgia facialis vera is characterized by pain in the distribution of the various divisions of the geniculate system. It may manifest itself as earache and as deep facial neuralgia. Geniculate prosopalgia is characterized by deep-seated pain in the face in the posterior orbital, nasal, malar and palatal regions, associated with pressure pain sensations. There are associated otalgia and referred pains in the mastoid and the occipital region, at times extending to the neck and the shoulder.

In some cases geniculate otalgia predominates; in others deep prosopalgia is more in evidence. This is in harmony with neuralgia of the other mixed cranial nerves—the fifth, ninth and tenth—in which partial and incomplete forms are encountered.

I have used the term deep prosopalgia not only because it expresses the essential nature and localization of the pain but in order to place it in contrast with the prosopalgia of trigeminal origin, which is more superficial and with which it has been confused.

It is thirty years since I described geniculate neuralgia, and many cases have been recorded, especially of the reflex and secondary (postherpetic) types.

It has been recognized and described in numerous monographs on neuralgia;[49] yet there has been but one case, that of Clark and Taylor, in which an operative procedure for geniculate neuralgia, with success, has been reported. This is the more remarkable, as twenty cases of glossopharyngeal neuralgia, which was recognized much later, are on record, in many of which relief was obtained by surgical intervention. Even in the field of the vagus nerve, superior laryngeal neuralgia is recognized and has been successfully treated with surgical measures.[50] Why has the treatment of geniculate neuralgia lagged behind in the general advance which has characterized the management of neuralgias of the other cranial nerves?

One reason, I believe, is the vestigial and obscure nature of its sensory system, which in the course of evolution has gradually receded before the advances of the trigeminal system, and has made its recognition difficult. This cannot have been a potent factor, as a fairly accurate description of the geniculate system was a part of my original report, which was adequate to support the concept of a neuralgic syndrome.

Another factor may have been the early criticisms of Mills[51] and Kidd,[52] who defended the traditional view of the facial nerve and opposed my newer conception of its sensory function. This, again, could not have played any considerable rôle, as through the years there has accumulated a considerable body of literature endorsing my views on the geniculate ganglion syndrome and geniculate neuralgia.

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49. (*a*) Harris, W.: Neuritis and Neuralgia, London, Oxford University Press, 1926, chap. 15. (*b*) Bailey, P.: Neuralgias of the Cranial Nerves, S. Clin. North America **11**:61, 1931. (*c*) Wexberg, E.: Neuralgien, in Bumke, O., and Foerster, O.: Handbuch der Neurologie, Berlin, Julius Springer, 1936, vol. 9, p. 206. (*d*) Cushing.[48]

50. Reichert, F. L.: Neuralgias of the Head and Face, Am. J. M. Sc. **187**: 362, 1934. Echols, D. H., and Maxwell, J. H.: Superior Laryngeal Neuralgia Relieved by Operation, J. A. M. A. **103**:2027 (Dec. 29) 1934. Halphen, E.: La nevralgie du nerf laryngé supérieur, Médecine **8**:289 (Jan.) 1927. Hutter, F.: Ueber Neuralgien des Nervus laryngeus superior, Monatschr. f. Ohrenh. **63**:402 (April) 1929.

51. Mills, C. K.: The Sensory Functions Attributed to the Seventh Nerve, J. Nerv. & Ment. Dis. **37**:273, 1910.

52. Kidd, L. J.: The Alleged Sensory Cutaneous Zone of the Facial Nerve in Man, Rev. Neurol. & Psychiat. **12**:393, 1914.

I believe that the real reason for the slower recognition of this neuralgic syndrome is that it has been masked by trigeminal and atypical facial neuralgia.

A neuralgic pain in the face was referred as a matter of course to the trifacial nerve, and it was only as experience accumulated that it became apparent that there are other types of pain not related to the gasserian system, some of which are certainly of geniculate origin. As I have already stated, I believe that many instances of geniculate neuralgia are concealed in the large group of cases of atypical facial neuralgia.

In the early history of glossopharyngeal neuralgia this was at first confused with trigeminal neuralgia; later it was mistaken for geniculate neuralgia.[53] The more careful delineation of the clinical picture has finally made its differentiation relatively easy. It is my belief that the same will be true of geniculate neuralgia, now that its anatomic distribution and clinical relations are more definitely established.

It would indeed be strange if the fifth, ninth and tenth cranial nerves had important relations to neuralgia and not the seventh nerve. Its exposed situation and the relation of the facial sensory system to the bony orifice and canals, the ear, the nose and throat and the paranasal sinuses seem to render it particularly vulnerable to neuritic and neuralgic affections.

A thought occurs in regard to the possibility of surgical intervention in this group of cases, in which many difficulties in diagnosis are presented. It will be recalled that Reichert in his case of tympanic plexus neuralgia used the Dandy method of approach, with the patient under local anesthesia, which exposes the fifth, seventh, ninth and tenth cranial nerves. He was then able to identify the affected nerve by touching it gently, which induced the neuralgic pain; this procedure served to differentiate the condition from geniculate otalgia with which it had originally been confused. This method, according to Bailey,[49b] was first used by Davenport in a case of glossopharyngeal neuralgia and should be invaluable for the confirmation of clinical evidence in a case in which the diagnosis is doubtful.

To summarize, the neuralgic affections of the various cranial nerves are: 1. True trigeminal neuralgia, which is distributed in one or more branches of the trifacial nerve and in which the pain is localized in the more superficial structures of the face and intra-oral region. This is classic prosopalgia or trifacial neuralgia. In cases of neuralgia of the third division of the fifth nerve there is often associated otalgia.

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53. Harris, W.: Some Experiences with Alcohol Injection in Trigeminal and Other Neuralgias, J. A. M. A. **63**:1725 (Nov. 14) 1914.

2. Geniculate neuralgia, which involves the deeper structures of the face. This is characterized by pain in the deep posterior orbital, palatal and nasal regions, with painful pressure sensation in the face. This is geniculate deep prosopalgia, and with it there is associated geniculate otalgia.

3. Glossopharyngeal neuralgia, which is characterized by neuralgic pains in the distribution of the glossopharyngeal nerve at the base of the tongue and the adjacent regions of the throat and by associated otalgia.

4. Superior laryngeal neuralgia, of vagal origin, in which the pains are localized in the region of the larynx, with associated otalgia.

All these various forms are accessible to surgical intervention by the cranial method of approach through the posterior fossa, which exposes the fifth, seventh, ninth and tenth cranial nerves. If this procedure is carried out with the use of local anesthesia, it is possible by touching any one of the nerves to reproduce the neuralgic pain, thus confirming the clinical diagnosis, which is often involved and difficult.

NEUROLOGIC MANIFESTATIONS IN VITAMIN G (B_2) DEFICIENCY

AN EXPERIMENTAL STUDY IN DOGS

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A vast amount of experimental work has been done in the attempt to elucidate the rôle of dietary deficiencies in nervous disorders. No attempt will be made in this paper to review adequately the many important contributions in this field. However, no paper dealing with this subject can neglect mention of Eijkman,[1] who in 1897 first described noninflammatory atrophic degeneration of the medullary sheaths of the peripheral nerves in hens fed polished rice. Since Eijkman's day, knowledge of deficiency diseases in general and of vitamin deficiencies in particular has been greatly advanced. It is now believed that there are at least three vitamin factors, in addition to other principles, which are essential for maintenance of the health of the nervous system. From the experimental standpoint, lesions in the nervous system have been produced through the absence of (*a*) the fat-soluble vitamin A, the precursor of which is carotene, (*b*) the water-soluble, heat-labile antineuritic vitamin B or B_1 and (*c*) the water-soluble, heat-stable vitamin G or B_2.

With respect to vitamin A deficiency, the work to date seems to indicate that a lack of this essential factor produces degeneration of the medullary sheaths of the peripheral nerves and of the ascending, chiefly the spinocerebellar, tracts of the spinal cord (Mellanby [2] and Zimmerman [3]).

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1. Eijkman, C.: Eine Beri Beri-ähnliche Krankheit der Hühner, Virchows Arch. f. path. Anat. **148**:523, 1897.

2. Mellanby, E.: The Experimental Production of Degeneration in the Spinal Cord, Brain **54**:247 (Sept.) 1931.

3. Zimmerman, H. M.: Lesions of the Nervous System in Vitamin Deficiency: I. Rats on a Diet Low in Vitamin A, J. Exper. Med. **57**:215 (Feb.) 1933.

In recent years it has been found that what had hitherto been called vitamin B is really a mixture of at least two components, namely, the heat-labile antineuritic factor and a thermostable substance, the absence of which was thought to produce pellagra. In dogs subsisting on a ration deficient in vitamin B (B_1) symptoms of the deficiency were found by Zimmerman and Burack [4] to develop within from sixty to ninety days. The first symptom is dragging of the hindlegs, which remain extended, so that the typical reflex of extensor-flexor alternation is not present in the gait. The spastic extension of the hindlimbs becomes more and more marked, and later incoordination also becomes manifest. The spastic paralysis progresses cephalad; marked opisthotonos appears; tonic spasms develop, and finally severe generalized convulsions occur. The periods of clonic spasm, which recur intermittently between periods of relaxation, are not unlike those associated with strychnine poisoning. The anatomic changes consist of extensive demyelinization of the sciatic, median, ulnar and vagus nerves and the brachial plexuses. Some animals displaying marked symptoms of this deficiency disease were treated with a specially prepared concentrate from rice polishings (vitamin B [B_1]). This resulted frequently in sudden, almost miraculous relief of symptoms even in the sickest animals, which would otherwise have succumbed in less than seven days. The therapy was found to be equally effective for periodic amelioration of symptoms developing over a longer time with the diet deficient in vitamin B_1. In this way it was possible to approximate more nearly the deficiency disease occurring in man (beriberi). Dogs in which the chronic deficiency state developed showed demyelinization of the peripheral nerves and minimal lesions of the same variety in the columns of Goll. However, the spinal lesions were not similar in distribution to those of "combined system disease" associated with pernicious anemia in man.

As a result of their studies, Goldberger and his associates [5] suggested that the disease blacktongue in dogs is the analog of pellagra in man and that this condition is essentially the result of dietary deficiency, probably lack of vitamin G. On the diet advocated by Goldberger, consisting largely of ground corn and ground cow-peas, Zimmerman, Cowgill, Bunnell and Dann [6] found that the well known picture of

4. Zimmerman, H. M., and Burack, E.: Lesions of the Nervous System Resulting from Deficiency of the Vitamin B Complex, Arch. Path. **13**:207 (Feb.) 1932.

5. Goldberger, J.; Wheeler, G. A.; Lillie, R. D., and Rogers, L. M.: A Further Study of Experimental Blacktongue with Special Reference to the Blacktongue Preventive in Yeast, Pub. Health Rep. **43**:657 (March) 1928.

6. Zimmerman, H. M.; Cowgill, G. R.; Bunnell, W. W., and Dann, M.: Studies on the Nervous System in Deficiency Diseases: Experimental Black Tongue, Am. J. Physiol. **109**:440 (Sept.) 1934.

blacktongue developed in dogs within from sixty to one hundred and fifty days. When the animals survived one hundred and twenty days or more, slight degenerative changes were observed in the medullary sheaths of the peripheral nerves and in the posterior columns at all levels of the cord. The uncertainties of the dietary regimen employed by Goldberger suggested that the effects produced were due to multiple factors. To control these and to study the sole effect of vitamin G deficiency, adult dogs were maintained by Zimmerman and Burack [7] on an artificial diet devised by Cowgill, which was believed to be adequate in all dietary essentials except vitamin G. In these animals there developed a slowly progressive disease characterized by loss of weight, vomiting, diarrhea and muscular weakness, which ended fatally in from two hundred to over three hundred days. Some of the animals presented the picture of sudden collapse, which could be controlled in rare instances by prompt subcutaneous administration of vitamin G in the form of liver extract. The anatomic changes in this condition consisted of marked destruction of the medullary sheaths of the peripheral nerves, degeneration of the medullary sheaths of the posterior and less often of the anterior nerve roots of the cord and degeneration of the medullary sheaths of the posterior columns and replacement by gliosis. The clinical and pathologic features of this condition are quite different from those characterizing the disease in dogs known as blacktongue. These experimental results indicate that in the Goldberger diet there is some other deficiency causing the rapid progression of the disease "blacktongue," with its dermatitis and buccal lesions. Such a factor has recently been suggested as occurring in association with the vitamin B complex (B_1 and B_2) and has been termed the "x" factor.[8]

In these experiments [7] only after the completion of the anatomic study of the nervous system was the fact revealed that degeneration of the posterior columns was as extensive and characteristic as the lesions of the peripheral nerves. Owing to the marked muscular weakness, which was frequently acute, the question of incoordination had not been satisfactorily studied. The work of Gildea, Kattwinkel and Castle [9] indicated that the administration of minimal amounts of vitamin G to the basic ration might forestall the appearance of "sudden collapse" and

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7. Zimmerman, H. M., and Burack, E.: Studies on the Nervous System in Deficiency Diseases: II. Lesions Produced in the Dog by Diets Lacking the Water-Soluble, Heat-Stable Vitamin B_2 (G), J. Exper. Med. **59**:21 (Jan.) 1934.

8. Block, R. J., and Hubbell, R. B.: Studies on the Vitamin B Complex: Further Indications for the Presence of a Third Factor, Yale J. Biol. & Med. **8**: 169 (Dec.) 1935.

9. Gildea, E. F.; Kattwinkel, E. E., and Castle, W. B.: Experimental Combined System Disease, New England J. Med. **202**:523 (March 13) 1930.

permit the development of a more chronic neurologic disease. Also the inanition factor in the preceding study obviously needed rigid control. The present experiment was devised for these purposes.

EXPERIMENTAL PROCEDURE

All the animals were kept on probation for a period of four weeks, during which an excessive amount of whole yeast (2 Gm. per kilogram of body weight) was given daily to insure a uniform nutritional history with respect to the vitamin B complex. Studies of the blood and analysis of the gastric contents were made in each case to establish a normal base line. Dogs with poor appetites were discarded. During this preliminary stage of the experiment each animal was taught to walk on his hindlegs, perform on an obstacle board and maintain his balance on a turntable. A normal neurologic status was demonstrated, and in some instances cinematographic records of the animal's behavior were obtained. All animals were given a vermifuge before starting the experiment.

TABLE 1.—*Artificial Ration Deficient in Vitamin G (B_2)*

Basal Mixture Constituents	Percentage
Casein (vitamin-free)*	30.0
Sucrose	36.0
Bone ash	4.0
Crisco	26.9
Salt mixture (Osborne-Mendel) including copper and manganese	3.0
Linoleic acid	0.1

The basal ration given above was supplemented with: vitamin B_1 concentrate (Block and Cowgill) from rice polishings, at least 1 pigeon unit per kilogram a day, and vitamins A and D in cod liver oil concentrate (White's), at least 1 tablet for each dog a day.

* Furnished by Dr. G. C. Supplee, of the Dry Milk Company, Bainbridge, N. Y.

Diet Employed.—The basal diet employed in this study consisted of an artificial ration which was palatable to the dog and adequate in all known dietary essentials except water-soluble, heat-stable vitamin G (B_2). The composition of this ration is shown in table 1. This mixture furnishes approximately 5 calories per gram. It was mixed with a known quantity of water and was offered as a gruel. Each dog was fed according to his estimated energy requirement; the kilogram unit scheme [10] followed in designing the ration insures that when the requisite calories are fed all the specific nutrients needed will be provided.

A record of the amount of food consumed daily was kept throughout the experiment as a gage of the appetite and an indication for the administration of the antineuritic vitamin B_1 concentrate. This concentrate was administered by mouth to all the dogs twice a week (1 pigeon unit [11] per kilogram of body weight per day) in the form of a concentrate [12] prepared from rice polishings by the

10. Cowgill, G. R.: An Improved Procedure for Metabolism Experiments, J. Biol. Chem. **56**:725 (July) 1923.

11. Block, R. J.; Cowgill, G. R., and Klotz, B. H.: The Antineuritic Vitamin: I. The Method of Assay, Concentration of the Vitamin with Silver Under Various Conditions, and Its Solubility in Certain Organic Solvents, J. Biol. Chem. **94**:765 (Jan.) 1932.

12. The concentrate was furnished by Eli Lilly and Company.

method of Block and Cowgill.[13] When oral administration appeared to be ineffectual, owing to vomiting or diarrhea, a commercial vitamin B_1 concentrate[14] was injected intramuscularly in at least twice the oral dose. A cod liver oil concentrate[15] was administered in tablet form daily to each dog.

Grouping of Animals.—A total of twenty-seven dogs was employed in the experiment. The animals were divided into nine groups of three dogs each, according to the amount of vitamin B_2 (G) added to the basal diet. This was given in the form of a powdered liver extract,[16] which contains, in addition to the well known hematopoietic factor, a liberal amount of vitamin B_2 (G) (from 6 to 7 Sherman-Borquin units per gram). A plan of feeding was also devised to control the inanition factor.

Group I: Three dogs were allowed to subsist on the basal ration completely deficient in vitamin G until they succumbed. The experimental situation was the same as that reported previously by Zimmerman and Burack.[7]

Group II: Three dogs served as inanition controls for group I. Each animal was offered only the amount of the basal ration eaten by its partner of group I on the preceding day. However, these animals received of the liver extract in powder form[16] 0.1 Gm. per kilogram of body weight daily.

Group III: These dogs received the basal ration supplemented with a minimum amount of liver extract (0.05 Gm. per kilogram daily). The purpose was to prevent, if possible, the sudden collapse which usually occurs in untreated animals. During the prolonged period of survival it was hoped that a more satisfactory study of the neurologic status could be made.

Group IV: The dogs in this group were the inanition controls for group III. Each animal was offered only the amount of the basal ration eaten by its partner of group III on the preceding day. The diet was supplemented with liver extract (0.1 Gm. per kilogram daily).

Group V.: The animals were allowed to subsist on the vitamin G deficient ration until symptoms of nerve lesions appeared, when they were treated with adequate amounts of the liver extract (0.1+ Gm. per kilogram daily).

Group VI: These dogs were the inanition controls for the animals in group V. Each animal was offered only the amount of the basal ration eaten by its partner of group V on the preceding day. The diet was supplemented with adequate amounts of vitamin G (0.1 Gm. per kilogram daily) throughout the experiment.

Group VII: Three dogs were maintained on the ration deficient in vitamin G, supplemented with 0.05 Gm. of liver extract per kilogram daily. This group corresponded in every way with group III and it was hoped that it would supply additional animals with the chronic deficiency state.

Group VIII: These animals were maintained under the same conditions as those of groups III and VII but were treated with the Block B_2 concentrate,[17]

13. Block, R. J., and Cowgill, G. R.: The Antineuritic Vitamin: III. Removal of Impurities by Fractional Precipitation, J. Biol. Chem. **97**:421 (Aug.) 1932.

14. Stuart, E. H.; Block, R. J., and Cowgill, G. R.: The Antineuritic Vitamin: V. The Preparation of a Vitamin Concentrate Suitable for Parenteral Use, J. Biol. Chem. **105**:463 (June) 1934.

15. White's cod liver oil concentrate was furnished by the Health Products Company, Newark, N. J.

16. Liver extract-Lilly was used.

17. This is the material prepared by Block from liver and is referred to in this paper[8] as product D used in the feeding experiments.

1 cc. daily, when symptoms appeared. The Block B_2 concentrate, devised especially for this experiment, consists of relatively pure vitamin G and is devoid of the x factor, as well as of many of the extraneous unknown substances of protein nature present in liver extract. The substitution of this concentrate for the liver extract might exhaust the x factor supplied by the latter substance, thereby permitting a study of the relation, if any, between the x factor and blacktongue.

Group IX: Three animals used as positive controls were allowed to subsist on the artificial ration supplemented with an adequate amount of liver extract throughout the experiment (0.1 Gm. per kilogram daily).

Clinical Observations.—Each dog was inspected daily at feeding time. The condition of the hair and tongue was noted. Careful records were kept of the appetite and of gastro-intestinal symptoms, such as vomiting or diarrhea. Each day a number of the animals were exercised, and the ability to walk on their hindlegs, perform on the obstacle board and maintain their balance on the turntable was noted. Whenever signs of weakness or incoordination appeared, a detailed neurologic examination was made. The deep reflexes were tested; the response to pinprick in the extremities was estimated and compared proximally and distally, and the degree of incoordination was further demonstrated by watching the animal shake when his neck was wet. A cinematographic record was also obtained of the motor disorder in each case.

Pathologic Studies.—The surviving animals, as a rule, were killed with chloroform. In all instances a complete necropsy was performed immediately after death. The thoracic and abdominal viscera were examined both grossly and microscopically. The median, ulnar, sciatic and tibial nerves, portions of the brachial plexus and the brain and spinal cord were fixed immediately on removal in 95 per cent alcohol, a dilute solution of neutral formaldehyde U. S. P. (1:10) and Müller's solution (without formaldehyde). Microscopic examination of this material was made as a routine in each case; in some instances additional nerves, such as the vagus, phrenic, femoral, saphenous and peroneal, were examined. Sections from the brain were stained with toluidine blue and by the Marchi and Kulschitzky methods. The spinal cords and peripheral nerves were stained as already described and also by the Alzheimer-Mann and Bielschowsky method and with sudan III.

Additional Data.—The blood, bone marrow, gastric secretion and blood sugar were studied in all animals. The results of these investigations will form the subject of a separate communication.

EXPERIMENTAL RESULTS

The more important data relating to the entire series of twenty-seven animals are summarized in table 2. The experimental results can be analyzed by comparing the clinical and pathologic observations for the different groups.

Animals Deprived of Vitamin G (Groups I and V).—These six dogs received no liver extract at the beginning of the experiment. Four collapsed suddenly and died, and the other two also succumbed. The average duration of life of these animals was only one hundred and seventy-five days, and the average loss of weight during the experiment was 3.1 Kg. Three of the dogs had definite neurologic signs,

which were confirmed by the observation of degenerative lesions in the nerves and posterior columns of the spinal cord at necropsy (dogs 115, 117 and 129).

Animals Receiving Minimal Amounts of Vitamin G (Groups III, VII and VIII).—Nine dogs received liver extract in inadequate doses

TABLE 2.—*Summary of Experimental Results*

Group	Dog, No.	Weight, Kg.		Liver Extract per Kg. Daily		Signs of				Duration of Experiment, Days	Died or Killed	Pathologic Lesions	
		Initial	Term	0.05 Gm.	0.1 Gm.	Bloody Diarrhea	Sudden Collapse	Weakness	Incoordination			Nerves	Posterior Columns
I	113	6.3	3.8	0	0	—	+	—	—	157	D	±	—
I	115	7.5	5.5	0	0	+	—	+	+	235	D	++	++
I	117	7.2	3.5	0	0	+	+	+	—	135	D	++	++
II	114	9.1	6.6	..	+	—	—	—	—	160	K	—	—
II	116	9.2	8.0	..	+	—	—	—	—	240	K	±	—
II	118	7.2	7.0	..	+	—	—	—	—	138	K	—	—
III	119	7.7	6.4	+	Started 337th day	+	—	++	++	415	K	++	++
III	121	9.4	7.5	+	0	—	—	—	—	372	D	+	+
III	123	6.2	5.3	+	Started 285th day	+	—	+	?	599	K	+	+
IV	120	9.3	9.0	..	+	—	—	—	—	415	K	—	—
IV	122	10.5	8.3	..	+	+	—	—	—	447	K	—	—
IV	124	11.8	12.3	..	+	—	—	—	—	652	K	—	—
V	125	9.0	5.6	0	0	+	+	—	—	182	D	—	—
V	127	7.4	5.0	0	0	—	+	—	—	107	D	±	±
V	129	9.2	4.5	0	Started 225th day	—	—	++	—	237	D	++	++
VI	126	6.9	5.0	..	+	—	—	—	—	182	K	—	—
VI	128	10.3	8.2	..	+	—	—	—	—	118	K	—	—
VI	130	7.2	7.2	..	+	—	—	—	—	338	K	±	—
VII	131	8.6	7.0	+	Started 285th day	+	—	++	?	350	K	++	++
VII	132	8.9	6.2	+	Started 265th day	++	—	—	—	330	K	+	+
VII	133	6.9	3.7	+	Started 191st day	—	—	++	++	226	K	++	++
VIII	134	6.0	3.5	+	*Started 126th day	++	—	++	+	164	D	+	+
VIII	135	6.1	5.1	+	"Block" 143rd day	—	—	—	—	329	K	+	—
VIII	136	9.4	7.2	+	"Block" 216th day	—	—	++	?	344	D	++	++
IX	137	3.7	6.4	..	+	—	—	—	—	405	K	—	—
IX	138	5.4	7.0	..	+	—	—	—	—	404	K	—	—
IX	139	7.4	9.3	..	+	—	—	—	—	393	K	—	—

* The dose was 0.075 Gm. per kilogram.

(0.05 Gm. per kilogram daily) at the beginning of the experiment. This minimal amount of vitamin G prevented sudden collapse in all instances, although three of the animals eventually died. The average duration of the experiment at death was two hundred and ninety-three days, whereas the average loss of weight of all nine animals during

this experiment was 1.9 Kg. In six of the dogs muscular weakness developed, and in three of these ataxia seemed to be definitely associated (dogs 119, 133 and 134). Degenerative nerve lesions were observed in every animal. The spinal cord was also involved in eight of the nine dogs. In four cases the pathologic changes were striking; in the other five they were less marked but definite.

The increase in the dosage of liver extract to a maintenance level (0.1 Gm. per kilogram daily) had a definite beneficial effect on the appetite and general health of the animal and obviously prolonged its life. However, the increase in amount of vitamin G did not cause any appreciable remission in the neurologic disease once it had developed. In the two animals which received the Block B_2 concentrate after the appearance of deficiency symptoms blacktongue did not develop.

Animals Used as Inanition Controls (Groups II, IV and VI).—All nine animals survived throughout the period of the experiment. Each dog was killed shortly after his experimental partner had died or was killed. These animals showed an average net loss of weight of 1.1 Kg., one having gained weight slightly. Only one of the group had bloody stools. In spite of insufficient food, they showed no signs of acute collapse, and no neurologic disorder developed. No lesions were observed except in two instances in which there were questionable changes in the peripheral nerves.

Animals Used as Positive Controls (Group IX).—All three dogs which received an adequate amount of vitamin G (0.1 Gm. per kilogram daily) remained vigorous and healthy throughout the experiment. They were killed on the average of four hundred days from the beginning of the experiment. There was an average gain in weight of 2.1 Kg. None of the animals showed neurologic signs, and necropsy disclosed no lesions in any instance.

CHARACTER OF THE NEUROLOGIC DISORDER

Altogether, in nine animals which had received an inadequate amount of vitamin G muscular weakness developed. This was chronic and distinct from the characteristic picture of sudden collapse seen in association with acute, untreated vitamin G deficiency. Two of these animals (dogs 119 and 133) also showed definite evidence of ataxia in the gait, and two others (dogs 115 and 134) were also thought to be unsteady in the upright posture. The incoordination was particularly striking in the case of dog 119. He assumed a broad base in standing and swayed and waddled when trying to run. He was too weak to support his weight on the hindlegs alone, as he had been trained, but with the front paws supported he was very unsteady, tending to stagger and fall whenever he was pushed gently. He was unable to shift his weight

properly. Ataxia was further revealed by the clumsiness of the animal's performance in attempting to hurdle the obstacle board, when he "overshot" with his hindlegs. He also had difficulty in maintaining his balance on the turntable, refusing to tread and at fast speed preferring to lie on his stomach and dig his claws into the board to prevent being swept off. The marked exaggeration of rapidly alternating movements while he was shaking himself was striking.

The muscular tone in the limbs of the weak animals seemed to be uniformly less than normal, except in one instance (dog 134). In no other case was spasticity demonstrable. The deep reflexes of the biceps, triceps, quadriceps, hamstring and gastrocnemius muscles were frequently diminished and were absent in two cases (dogs 119 and 133). The pectoral and psoas reflexes were less affected. Superficial pain sense (pinprick) was also thought to be diminished in the foot-pads and in the hindlimbs of a few of the affected animals.

The neurologic picture in the affected animals was sufficiently constant to indicate involvement of the peripheral neurons. The clinical problem was whether deep sensibility was cut off solely by the peripheral nerve lesion or whether the incoordination might be due to an added degenerative process in the posterior columns of the cord. In the presence of flaccid weakness the element of incoordination is difficult to evaluate, even when the animal has been previously trained. It is impossible to test the dog for loss of position and vibratory sense or to measure the extent or degree of distal cutaneous hypoesthesia. However, even when such an appraisal is made, as in man, it does not always enable one to diagnose a lesion of the cord in addition to peripheral neuritis.

CHARACTER OF THE PATHOLOGIC CHANGES

Of the entire group of fifteen animals which had received an inadequate amount of vitamin G, a total of twelve showed definite lesions. The nerves were involved in all twelve instances; in one case (dog 135) the spinal cord escaped. The anatomic changes consisted of the following: (*a*) Marked degeneration of the medullary sheaths and axis-cylinders of the peripheral nerves (figs. 1 and 2). The nerves of the hindlimbs were more severely involved than those of the forelimbs. The more distal portions of the nerves likewise suffered more than the proximal.

(*b*) Fairly common degeneration of the medullary sheaths of the posterior nerve roots, with less frequent involvement of the anterior roots of the cord.

(*c*) Degeneration of the medullary sheaths and axis-cylinders of the posterior columns of the spinal cord (figs. 3, 4, 5 and 6). This was

particularly striking in the fasciculus gracilis. The destroyed tracts were replaced in large part by glial tissue. The lesion extended through the entire length of the cord and was seen in eleven animals, including the four (dogs 115, 119, 133 and 134) in which incoordination had been definitely observed clinically.

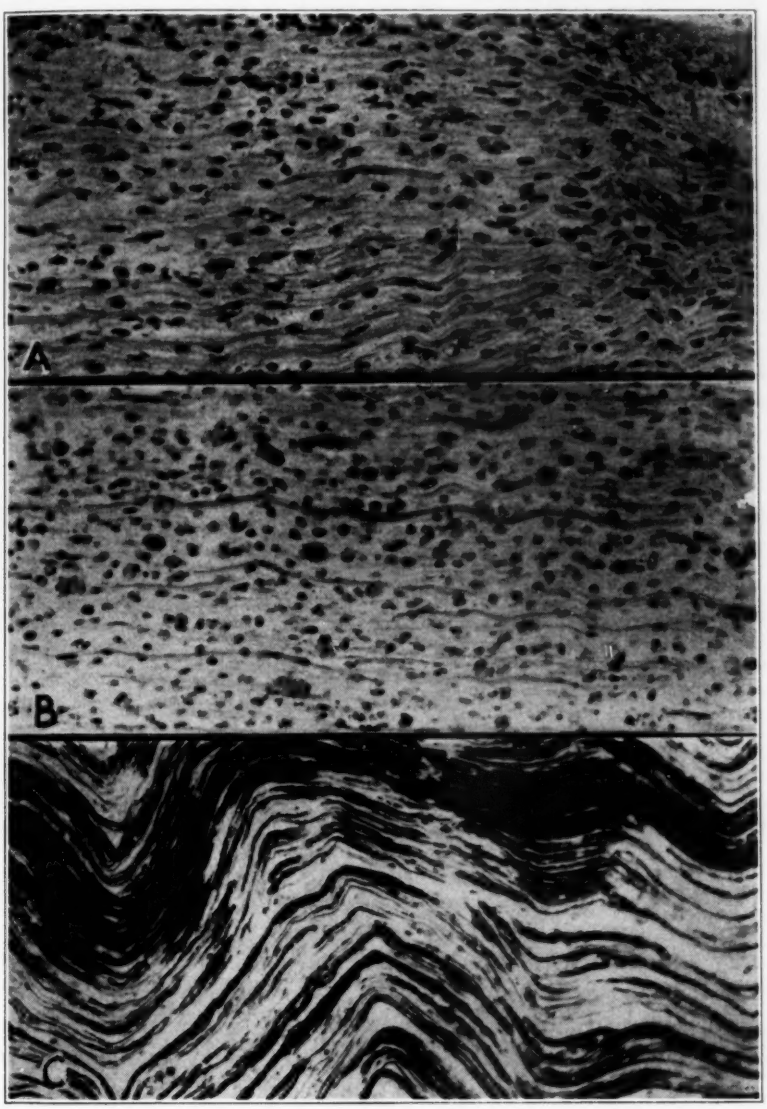

Fig. 1 (dog 119).—Photomicrographs (× 125) of the sciatic nerve, showing (*A*) the extent of accumulation of fat (sudan III stain), (*B*) another portion of the same nerve (Marchi stain) and (*C*) the extent of demyelinization of another portion of the same nerve (Kulschitzky stain).

The ganglion cells of the cerebral cortex, basal ganglia and spinal cord were spared. There was no demyelinization of the pyramidal tract in any instance. It should be noted that the degenerative lesions in the spinal cord and peripheral nerves in this experimentally produced nervous disease are similar to those which have been observed in many cases of human pellagra.

SUMMARY AND CONCLUSIONS

The basal diet employed in this study consisted of an artificial balanced ration which was palatable to the dog and adequate in all known

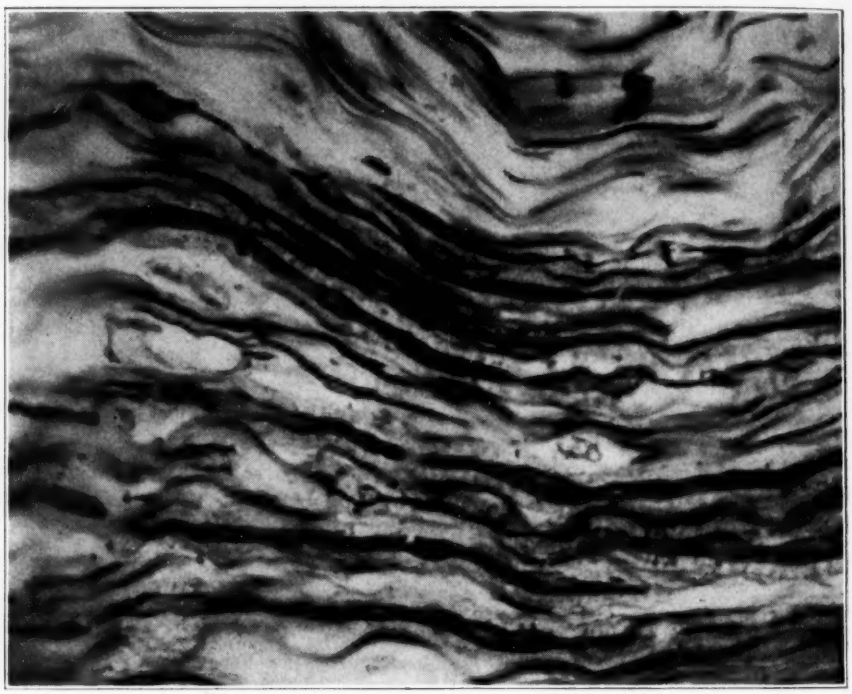

Fig. 2 (dog 119).—Photomicrograph of the sciatic nerve, showing fragmentation and swelling of the axis-cylinders. Bielschowsky stain; × 550.

dietary essentials except water-soluble, heat-stable vitamin G (B_2). The experiment was controlled by feeding a second group of dogs the same diet plus an adequate amount of vitamin G (0.1 Gm. of liver extract per kilogram of body weight daily). A third group of animals served as controls for the inanition factor; each animal was fed daily only as much of the basal ration as his experimental partner had eaten on the preceding day, plus an adequate amount of vitamin G.

During the first stage of the experiment the animals were taught to walk on their hindlegs, hurdle an obstacle board and maintain their

balance on a turntable. Repeated examinations of the neurologic status were made throughout the experiment, and frequent cinematographic records were obtained.

In twelve of the fifteen dogs maintained on the ration deficient in vitamin G a slowly progressive disease developed, characterized by loss of weight, vomiting and bloody diarrhea, flaccid muscular weakness, incoordination and decrease of the deep reflexes. Death occurred in from one hundred and seven to five hundred and ninety-nine days.

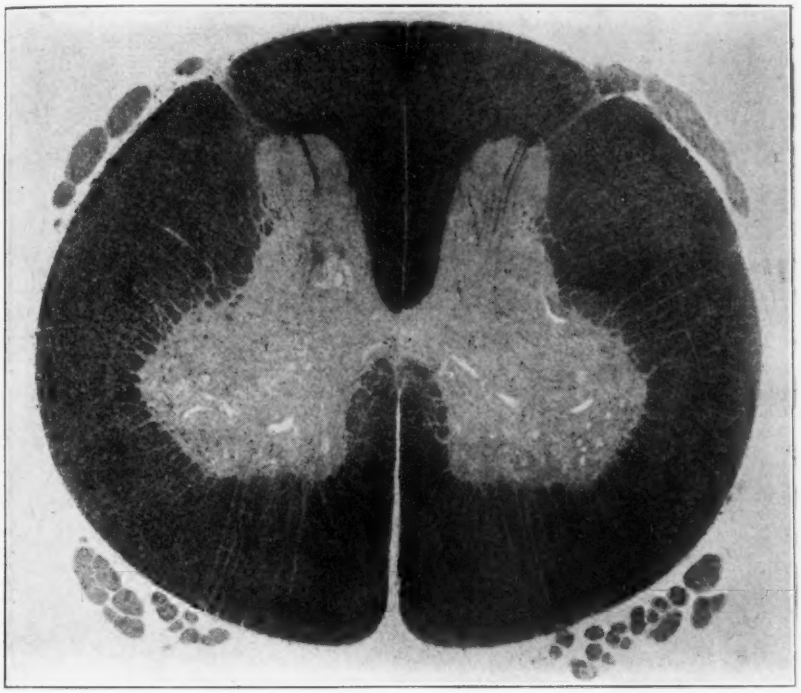

Fig. 3 (dog 119).—Cervical portion of the cord, showing the triangular area of accumulation of fat in the columns of Goll and the dispersion of fat particles in the columns of Burdach. Marchi stain; × 14.

It was found that the acute symptoms could be modified and the life of the animal prolonged by the administration of a minimal amount of vitamin G—0.05 Gm. of liver extract per kilogram of body weight daily. This permitted the gradual development of the neurologic signs to a more marked degree.

In each of the twelve control animals which received an adequate amount of vitamin G there failed to develop either the clinical or the pathologic manifestations of the disease.

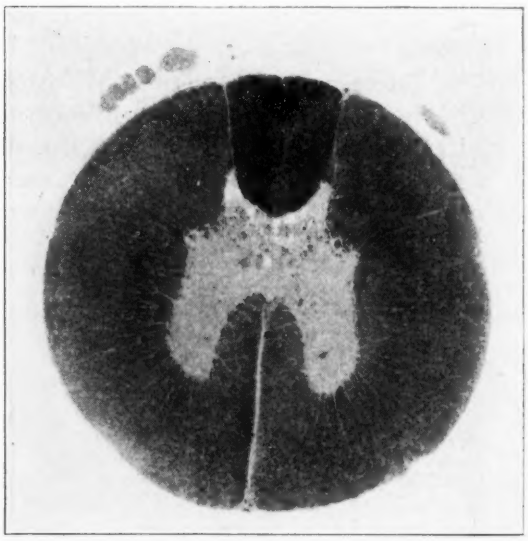

Fig. 4 (dog 119).—Thoracic portion of the cord, with accumulation of fat in the columns of Goll. Marchi stain; × 12.

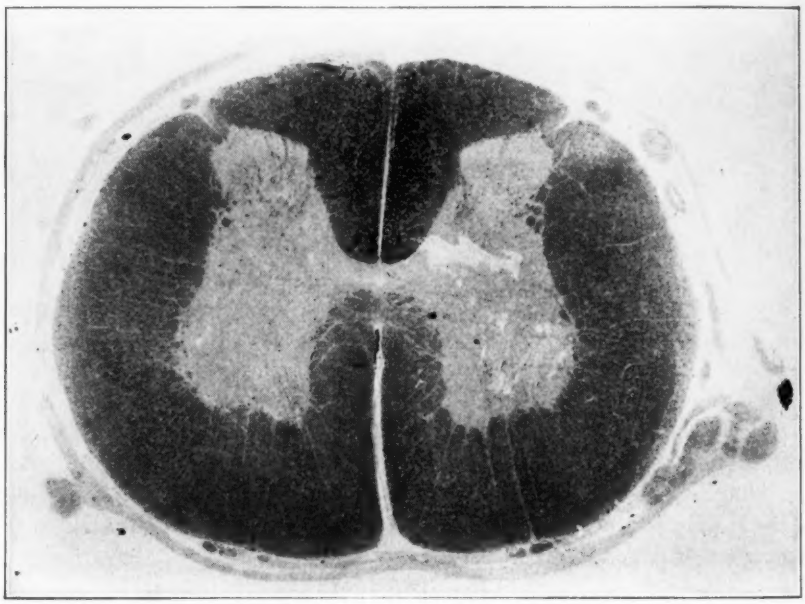

Fig. 5 (dog 119).—Lumbar portion of the cord, with fat particles in the posterior columns. Marchi stain; × 12.

The lesions consist of marked demyelinization of the peripheral nerves and degeneration of their axis-cylinders. Many medullary sheaths and axis-cylinders of the posterior columns are also destroyed and replaced by gliosis. These degenerative changes in the nervous system are similar to those observed in cases of human pellagra.

The clinical features of this condition are quite different from those characterizing the canine disease known as blacktongue. The latter has its onset in from sixty to one hundred and twenty days after the animal has been started on the Goldberger diet, which is probably deficient in a number of factors besides vitamin G.

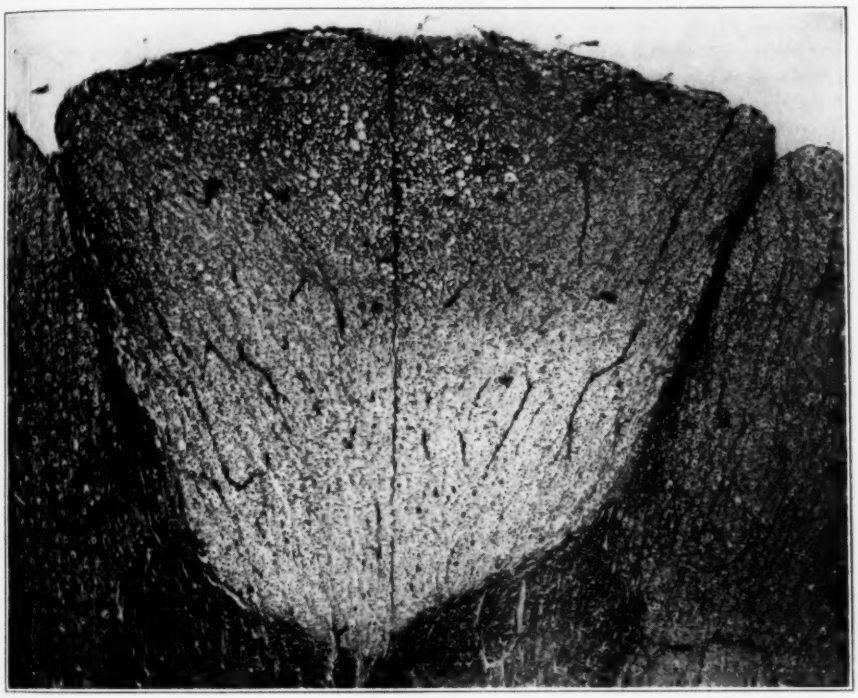

Fig. 6 (dog 119).—Photomicrograph of the posterior columns of the lumbar portion of the cord, showing loss of medullary sheaths and axis-cylinders. Alzheimer-Mann stain; × 62.

PROTOCOLS

Group I.—Dog 113.—A black and white female terrier, weighing 6.3 Kg., received no liver extract throughout the experiment. Anorexia and progressive loss of weight were the prominent symptoms. She died on the one hundred and fifty-seventh day of the experiment, after sudden collapse characteristic of acute, untreated vitamin G deficiency. The final weight was 3.8 Kg. Necropsy showed slight demyelinization of the peripheral nerves but no involvement of the spinal cord.

Dog 115.—A white male poodle, weighing 7.5 Kg., received no liver extract at any time. Bloody diarrhea was present intermittently. He was noted to drag the hindlegs slightly on the one hundred and sixty-first day of the experiment. On the one hundred and eighty-sixth day he was unsteady and tended to fall when attempting to walk on his hindlegs. He stood with a broad base and was clumsy on the obstacle board. The signs became more marked on the one hundred and ninety-eighth day. He died on the two hundred and thirty-fifth day; the final weight was 5.5 Kg. The pathologic changes consisted of demyelinization of the sciatic nerves and posterior columns of the spinal cord. The columns of Goll were noted to be more involved than those of Burdach. The lesions were seen only in the Marchi preparations.

Dog 117.—A female mongrel, weighing 7.2 Kg., while exercising on the one hundred and first day showed weakness, which increased during the next four weeks. Bloody diarrhea appeared on the one hundred and eleventh day and was repeated thereafter. Death followed sudden collapse on the one hundred and thirty-fifth day; the final weight was 3.5 Kg. Demyelinization of the sciatic nerves and brachial plexuses was demonstrable with all staining methods. The dorsomedian fasciculi of the spinal cord were degenerated and partly replaced with glial tissue.

Group II.—Dog 114.—A female mongrel, weighing 9.1 Kg., was the inanition control for animal 113. She was fed daily only as much of the basal ration as her experimental partner had eaten on the preceding day. However, she received an adequate amount of vitamin G in the form of liver extract (0.1 Gm. per kilogram daily) throughout the experiment. Her appetite was good and she remained well until she was killed with chloroform on the one hundred and sixtieth day. The final weight was 6.6 Kg. No lesions were observed in the peripheral nerves or the spinal cord.

Dog 116.—A white male Scotch terrier, weighing 9.2 Kg., served as the inanition control for animal 115 and remained vigorous and well in every respect until he was killed with chloroform on the two hundred and fortieth day. The final weight was 8 Kg. Necropsy revealed a few black granules in the sciatic nerves in the Marchi preparations; otherwise the nerves and spinal cord were normal.

Dog 118.—A female terrier, weighing 7.2 Kg., was the inanition control for animal 117. No symptoms developed until she was killed with chloroform on the one hundred and thirty-eighth day. The final weight was 7 Kg. Examination of the central and peripheral nervous system showed no lesions.

Group III.—Dog 119.—A black male terrier, weighing 7.7 Kg. received daily at the beginning of the experiment 0.05 Gm. of liver extract per kilogram of body weight. Vomiting began on the one hundred and eighteenth day and lasted for four days; bloody stools appeared on the one hundred and fifty-fourth day and were noted periodically thereafter. On the two hundred and fiftieth day the animal seemed unsteady in the upright posture. He made no voluntary effort to hurdle the obstacle board and was unstable in balancing on the hindlegs. Vitamin G was increased to an adequate amount on the three hundred and thirty-seventh day of the experiment (0.1 Gm. of liver extract per kilogram daily). Neurologic examination on the four hundred and seventh day revealed a flaccid ataxic gait, with broad base and waddle in walking. The incoordination was beautifully shown when the dog shook himself. The deep reflexes could not be obtained. The dog was killed with chloroform on the four hundred and fifteenth day, when he weighed 6.4 Kg. Necropsy showed marked destruction of the medullary sheaths and axis-cylinders in the peripheral nerves. The posterior columns of the spinal cord also

showed extensive destruction of the medullary sheaths, but the axis-cylinders were injured to a less degree. A glial scar replaced the posterior columns in large part.

Dog 121.—A tan female terrier, weighing 9.4 Kg., received a minimal amount of liver extract throughout the experiment (0.05 Gm. per kilogram). She remained well except for progressive loss of weight. There were no clinical signs indicating a nervous disorder at any time. She died on the three hundred and seventy-second day, weighing 7.5 Kg. Pathologic changes consisted of a moderate amount of degeneration of the peripheral nerves, shown with the sudan III and somewhat more with the Marchi stain. The lumbar portions of the spinal cord showed degeneration of the posterior columns with considerable replacement gliosis. The higher levels of the cord appeared normal.

Dog 123.—A white male Spitz, weighing 6.2 Kg., was given a minimal amount of liver extract from the start. Diarrhea appeared on the eighty-eighth day and became bloody on the one hundred and fifty-second day but subsequently disappeared. Because of the development of muscular weakness the amount of liver extract was increased to 0.1 Gm. per kilogram on the two hundred and eighty-fifth day. This apparently forestalled the subsequent development of clearcut neurologic signs. The animal survived until the five hundred and ninety-ninth day, when he was killed with chloroform. The final weight was 5.3 Kg. A moderate degree of demyelinization of the peripheral nerves and posterior columns of the spinal cord was observed at necropsy.

Group IV.—Dog 120.—A brown female spaniel, weighing 9.3 Kg., was the inanition control for dog 119 and was fed daily only as much of the basal ration as her experimental partner had eaten on the preceding day. However, she received an adequate amount of vitamin G in the form of liver extract (0.1 Gm. per kilogram daily). She remained well throughout the experiment and was killed on the four hundred and fifteenth day. The final weight was 9 Kg. The central and peripheral nervous systems were normal.

Dog 122.—A white male mongrel, weighing 10.5 Kg., was the inanition control for animal 121. Early in the experiment this animal had bloody stools on two occasions and lost weight. Otherwise, he remained healthy until he was killed with ether on the four hundred and forty-seventh day. The final weight was 8.3 Kg. Necropsy revealed that the central and the peripheral nervous systems were normal.

Dog 124.—A brown and white male collie, weighing 11.8 Kg., was the inanition control for animal 123. His health remained perfect as long as his experimnetal partner was allowed to live (five hundred and ninety-nine days). As a further measure of control he was allowed to live until the six hundred and fifty-second day, when he was killed with chloroform. The final weight was 12.3 Kg. Necropsy showed the peripheral and central nervous systems to be normal.

Group V.—Dog 125.—A brown and white female terrier, weighing 9 Kg., was given no liver extract at any time. A bloody stool appeared on the one hundred and thirtieth day. When she collapsed suddenly on the one hundred and eighty-first day, she was given 5 cc. of the commercial vitamin B_1 concentrate hypodermically and was kept warm. However, she had repeated convulsions and died on the following day. The final weight was 5.6 Kg. No lesions were observed in the peripheral nerves, spinal cord or brain.

Dog 127.—A tan female hound, weighing 7.4 Kg., was given no vitamin G and lost weight rapidly and steadily. She collapsed suddenly on the one hundred and seventh day and died in spite of the intramuscular administration of 4 cc. of the

commercial vitamin B_1 concentrate. The final weight was 5 Kg. Necropsy showed that an occasional peripheral nerve fiber and fasciculus in the posterior column was demyelinated. Otherwise, there were no pathologic changes.

Dog 129.—A black and tan male terrier, weighing 9.2 Kg., received no liver extract at the start of the experiment. The reflexes were noted to be hyperactive on the one hundredth day. Because of rather marked weakness on the one hundred and eighty-third day, the dog was given 0.2 Gm. of liver extract per kilogram daily for the next ten days. Weakness persisted, but the gait did not appear to be ataxic. Beginning on the two hundred and twenty-fifth day, the maintenance dose of liver extract was administered until his death, on the two hundred and thirty-seventh day. The final weight was 4.5 Kg. The sciatic nerves and brachial plexuses showed extensive demyelinization. The axis-cylinders were less involved. There was marked degeneration of the posterior columns, involving the median fasciculi more than the lateral. Glial tissue replaced the posterior columns in part.

Group VI.—Dog 126.—A tan and white female terrier, weighing 6.9 Kg., was the inanition control for animal 125 and was fed daily only as much of the basal ration as her experimental partner had eaten on the preceding day. She remained well until she was killed with chloroform, on the one hundred and eighty-second day. The final weight was 5 Kg. The central and peripheral nervous systems were normal.

Dog 128.—A black, tan and white female hound, weighing 10.3 Kg., was the inanition control for animal 127. She remained healthy throughout the experiment until she was killed, on the one hundred and eighteenth day. The final weight was 8.2 Kg. The peripheral nerves, spinal cord and brain showed normal histologic pictures.

Dog 130.—A black and white male terrier, weighing 7.2 Kg., was the inanition control for dog 129. His general health was vigorous until he was killed with chloroform, on the three hundred and thirty-eighth day, weighing 7.2 Kg. Necropsy showed a few black granules in the peripheral nerves stained by the Marchi method. Other microscopic preparations revealed nothing abnormal. The spinal cord and brain were normal.

Group VII.—Dog 131.—A black and white female hound, weighing 8.6 Kg. was given an inadequate amount of vitamin G, consisting of 0.05 Gm. of liver extract per kilogram daily. A bout of bloody diarrhea began on the one hundred and sixtieth day and lasted four days. At this time she was unable to hurdle on the obstacle board, was unsteady on the turntable and refused to walk on her hindlegs. The disorder continued throughout the experiment. The dose of liver extract was increased to 0.1 Gm. per kilogram on the two hundred and eighty-fifth day. She survived until the three hundred and fiftieth day, when she was killed with chloroform. The final weight was 7 Kg. Extensive degeneration involved the peripheral nerves. The columns of Goll and Burdach both showed degeneration throughout the entire length of the cord. A glial scar replaced these columns in part.

Dog 132.—A black and white male bull, weighing 8.9 Kg., was given a minimal amount of liver extract. Bloody diarrhea was noted on the eighty-sixth day and repeatedly thereafter. The dose of liver extract was increased to 0.1 Gm. per kilogram on the two hundred and sixty-fifth day. Repeated neurologic surveys revealed no definite signs. The animal was killed with chloroform on the three hundred and thirtieth day, when he weighed 6.2 Kg. Necropsy revealed a moderately advanced stage of degeneration of the medullary sheaths of the periph-

eral nerves and spinal cord. The posterior columns alone were involved and were largely replaced by a proliferative glial reaction. The median fasciculi were more involved than the lateral.

Dog 133.—A gray and black male terrier, weighing 6.9 Kg., received a minimal amount of vitamin G. He lost weight continually and began vomiting on the one hundred and seventy-second day. A few days later muscular weakness and an unsteady gait developed. When he attempted to walk on his hindlegs the gait was ataxic. The reflexes could not be obtained on the one hundred and eighty-seventh day. The dose of liver extract was increased to 0.1 Gm. per kilogram daily on the one hundred and ninety-first day, and the experiment was prolonged until the two hundred and twenty-sixth day, when the dog was killed with chloroform. The final weight was 3.7 Kg. The lesions in the peripheral nerves and spinal cord were best seen in the Kulschitzky preparations. These consisted of a loss of myelin in the peripheral nerves and the columns of Goll. The cord lesion was striking in the Alzheimer-Mann and the Nissl (toluidine blue) preparations.

Group VIII.—Dog 134.—A black and white female wire hair terrier, weighing 6 Kg., was given at the start of the experiment a minimal amount of liver extract. Loss of hair was noted on the one hundred and twenty-sixth day, and at this time the dose of liver extract was increased to 0.075 Gm. per kilogram daily. On the one hundred and fifty-second day the animal was weak, and within a few days the gait became definitely ataxic. She suffered from severe diarrhea and emaciation. During the two weeks prior to her death the hindlegs seemed to become progressively stiffer. She died on the one hundred and sixty-fourth day, weighing 3.5 Kg. The sciatic nerves and the brachial plexuses showed slight demyelinization; the columns of Goll also showed mild degeneration of the medullary sheaths. The pyramidal tracts were intact.

Dog 135.—A white female terrier, weighing 6.1 Kg., was given an inadequate amount of liver extract. She remained well until the one hundred and forty-third day, when the liver extract was substituted with 1 cc. of the Block B_2 concentrate daily by mouth. There were no manifestations of blacktongue during the subsequent six months of the experiment. Neurologic signs were absent. The animal was killed on the three hundred and twenty-ninth day, weighing 5.1 Kg. Striking degenerative lesions were demonstrated in the Marchi preparations of the peripheral nerves. Less, but definite, evidence of degeneration was seen in the sudan III preparations. The spinal cord and the brain were normal.

Dog 136.—A female brindle terrier, weighing 9.4 Kg., received a minimal amount of liver extract. On the one hundred and sixty-ninth day she was unable to perform on the turntable or hurdle over the obstacle board. Weakness was obvious, but the ataxia was uncertain. On the two hundred and sixtieth day she was given 1 cc. of Block B_2 concentrate daily by mouth. During the remaining four months of life there were no symptoms of blacktongue. She died on the three hundred and forty-fourth day, weighing 7.2 Kg. There was marked degeneration of the medullary sheaths of the sciatic nerves and brachial plexuses. About 50 per cent of the fibers were destroyed. The columns of Goll and Burdach were both involved in the degenerative process, but the former suffered to a greater degree. Gliosis was seen in the posterior columns in the Nissl preparations.

Group IX.—Dog 137.—A tan and white, adult male terrier, weighing 3.7 Kg., received, in addition to the basal ration, an adequate amount of vitamin G from the beginning of the experiment (0.1 Gm. per kilogram daily). He gained weight continually and remained vigorous and healthy throughout. When he was killed with chloroform on the four hundred and fifth day, the final weight was 6.4 Kg. The central and peripheral nervous systems were normal.

Dog 138.—A tan and white, adult female poodle, weighing 5.4 Kg., was given an adequate amount of liver extract. She gained weight and was entirely free from symptoms throughout the experiment. She was killed with chloroform on the four hundred and fourth day; the final weight was 7 Kg. The peripheral nerves, spinal cord and brain were all normal.

Dog 139.—A tan and white male terrier, weighing 7.4 Kg., was given an adequate amount of liver extract. He remained healthy for three hundred and ninety-three days, when he was killed with chloroform. The final weight was 9.3 Kg. The peripheral and central nervous systems were normal.

DISCUSSION

Dr. I. S. Wechsler, New York: These experiments are of interest for the reason that the feeding was done precisely. A great many animal experiments are not carried on in this manner, and it is difficult to tell which vitamin is deficient, even though attempts are made to feed the animals according to various formulas. In this particular instance the attempt was made and well carried out, in that only part of vitamin B, namely, vitamin G, was deficient in the feeding. Whether this has any clinical application is another question.

In some of the experiments on monkeys, which will be described presently, my colleagues and I did not obtain the same results, and when it comes to human subjects it is extremely difficult to carry out any experimental feeding. One knows that even a so-called well balanced diet may be deficient in various vitamins, and one does not always know, even though a formula is followed, the extent or kind of vitamin privation that results. It is not alone the vitamin B complex which causes degeneration of the central nervous system; certainly, vitamin A privation also causes it. It is a question whether vitamins C and D also do not; that vitamins B and A cause it is now certain.

The question, too, arises whether there is selective affinity of the vitamins for certain parts or pathways of the nervous system. The great difficulty is that so little is known about the chemistry of the nervous system. It is certain that there is selectivity. Despite the fact that the fibers seem to be the same in various pathways, apparently there is some chemical difference that causes a response in a selective way to the presence of various drugs, toxins, viruses, proteins and foods.

The question in my mind is whether it will not be possible by these and other chemical studies to define once and for all what is meant by the word degenerative. At present the word is commonly used, but it is impossible to define it. It is known that disappearance of myelin, fragmentation and breaking up of axis-cylinders and replacement with glial tissue occur, but these are merely descriptive terms. Many degenerative diseases of the nervous system have apparently similar or fairly similar pathologic substrata as the result of various factors, but whether these are due to vitamin privation, an infection, a virus or some other factor is not known.

I think that this paper is unusually interesting particularly because of the preciseness with which the experiments were carried out.

Dr. B. R. Tucker, Richmond, Va.: I feel that this is a valuable paper, but I do not believe that the pathologic changes noted in the spinal cord are closely related to those noted in human pellagra. I have made a study of six spinal cords and two chains of spinal sympathetic ganglia from patients with pellagra. The lesions seem to me to be different from those that have been shown here. I think that further study should be made of vitamin deficiency in pathologic

changes of the nervous system. It is likely that pellagra may be due to a virus infection rather than to vitamin deficiency. I believe that Goldberger's idea has contributed greatly to the knowledge of susceptibility to the disease.

I wrote to six southern hospitals in which there were many patients with pellagra and in which a pellagra-preventive diet was used. Dr. David Wilson of the University of Virginia has included the lesions of pellagra in his study of virus diseases. It was observed that the chief lesions were gliosis, degeneration, misshapen cells and chromatophils in the posterior horn cells toward the lateral aspect of the cord. Unfortunately, I did not make a study of the peripheral nerves. I did, however, make a study of two posterior spinal sympathetic ganglia and observed that they were markedly degenerated.

The diet that is supposed to be pellagra preventive includes various forms of milk, pork, liver, corn beef, salmon, haddock and other fish, kale, turnip tops, spinach, cabbage, green peas, green beans and tomatoes, but pellagra has developed in patients on this diet, which is the diet adopted by the United States Public Health Service. Dr. Blackford and Dr. Sebrell have preferred, instead of the term vitamin B_2 or vitamin G deficiency-preventive diet, the term pellagra-preventive diet, but this diet does not always prevent pellagra.

Yeast was introduced into the diet to prevent pellagra, and I think it had some good effect, but it does not always prevent pellagra. I have seen severe pellagra develop and continue while brewers' yeast was being used. Over great areas in China, Egypt and India a pellagra-inviting diet is commonly used, but pellagra is rare.

The question of the etiology of pellagra, of course, is not settled, but I believe it is much more likely to be a virus disease than a vitamin deficiency disease.

Dr. W. H. Harris, of the Tulane University of Louisiana School of Medicine, macerated the spinal cords and other organs of patients with pellagra and injected the material into monkeys producing spinal lesions, diarrhea, nervous symptoms and loss of weight. In a recent article on the effects of an excessive vitamin G or B_2 diet it was stated that this diet produced demyelinization in the central nervous system. Since changes occur as a result of both the deficiency and the increased diet, I think one should keep an open mind on this subject until further investigation has been made.

Dr. C. K. Russell, Montreal, Canada: It is extraordinarily interesting that in these experimental animals lesions developed in the dorsal portion of the spinal cord but I believe that one should be cautious about concluding that the results were due to a lack of vitamin G particularly. About forty years ago Edinger performed a similar experiment. He took animals in which a confrère had produced anemia, in an unsuccessful effort to cause subacute degeneration of the cord. Edinger made these animals run until fatigued, and in that way definite degeneration was produced not only in the peripheral nerves but in the dorsal columns of the cord. On that observation he based his theory of tabes dorsalis, to which I still feel this association has not given sufficient consideration. Edinger's exhaustion theory was that function creates the symptom complex. In debilitating conditions in which the recuperability of cells might be interfered with, the neurons which must function continuously or excessively become exhausted and are unable to sustain their long axis-cylinder processes. Atrophy of these processes follows.

Now, I wonder whether in these animals a similar condition had not been produced. These animals had been trained to go through movements which require the use of the sense of position, standing on the hindlegs, running on a turntable and other actions, which throw the extra amount of functioning on

the neurons which convey the sense of position particularly. One might ask why the ventral horn cells became degenerated. The ventral horn cells are normally constituted so that they may respond to two sets of stimuli, one from the cortex and one reflex, in the spinal cord, and when either of these sets of stimuli is not working, the neuron in the ventral horn has an opportunity to rest and recuperate, whereas the neurons which in functioning give the sense of position in the trunk and limbs have been excessively active. As a result these neurons have become exhausted, and their axis-cylinders have atrophied.

Dr. Israel Strauss, New York: An investigation of this nature is important and has great scientific value. However, I feel that when one attempts to utilize the conclusions and the inferences to be drawn from work of this type on animals for the human subject one is taking a step which has a certain amount of hazard. I believe that in judging the effect of diet on the human subject, one must consider the total personality.

Dr. Wechsler was one of the first to show that so-called neuritis, i. e., alcoholic neuritis, is not an inflammatory but a degenerative process. Probably he is correct, and one of the main factors in the production of this clinical syndrome is a diminution in vitamin ingestion. As a matter of fact, most physicians today in treating a condition of this kind are giving the patients a diet rich in vitamins. But neuritis does not develop in every alcoholic patient. Many of these patients unquestionably have ill balanced diets but do not acquire neuritis. As Dr. Wechsler says, many human beings take what appears to be a well balanced diet, yet vitamin deficiency develops. Stockard found that in one of his strains of dogs a balanced diet containing the usual requisite amount of calcium which had been fed to his other breeds of dogs successfully resulted in inanition and maldevelopment of the bones. In order to maintain that breed of dogs in perfect health, he had to add to the normal balanced diet an additional amount of calcium.

It seems to me, therefore, not only that certain tracts of the nervous system are possibly more susceptible to certain interferences than others but that each human being has certain tendencies or weaknesses, a certain constitutional set-up, which makes him more or less liable to deficiency and that the deficiency in the diet is not the sole cause of the vitamin deficiency syndrome.

Dr. E. D. Friedman, New York: A number of years ago I had the opportunity of seeing some of the patients with alcoholic neuritis at the Bellevue Hospital, and in a number of instances the diagnosis of alcoholic pseudopellagra (as it was called in those days) was made because the patient presented, in addition to the signs of polyneuritis, typical mental symptoms and pigmentation of the dorsa of the feet and hands, signs which were then commonly associated with the clinical syndrome of pellagra. It was always felt that there was a factor of vitamin deficiency in this syndrome. Every experienced psychiatrist will occasionally encounter a patient with involutional melancholia who has suffered from inanition with a deficient vitamin intake and presents the picture of "pseudopellagra."

It is both interesting and satisfying to have such excellent confirmation of these clinical impressions. These syndromes of which one was formerly vaguely cognizant have now received at least a sounder basis through this investigation of the rôle of the vitamins.

NEUROLOGIC ASPECTS OF PETROSITIS

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The intracranial complications of otitic and paranasal sinus disease are trying both to the otolaryngologist and to the neurologist. Localized and generalized meningitis, cerebral and cerebellar abscesses, sinus thrombosis and involvements of the facial, abducens and fifth nerves have been familiar for many years, and the Gradenigo syndrome became known as an entity in 1903.[1] Knowledge regarding the routes of invasion of the endocranium has been enriched by the investigations of Eagleton and others, but a great deal remains unknown about this important subject. In recent years there has come into prominence the involvement of the petrous tip, which presents interesting neurologic symptoms, and a study of this process helps in elucidating another route by which the central nervous system becomes involved. This subject has received a great deal of attention in otolaryngologic literature but little or no comment from neurologists. Having had trying experiences in cases of petrositis, seven of which are reported in this paper, we deemed it advisable to review the subject from a neurologic standpoint. The symptomatology of petrositis is peculiarly bound up with anatomic and pathologic considerations, and these will be discussed first.

ANATOMIC CONSIDERATIONS

It is important to bear in mind the fundamental gross relationships of the temporal bone. The external or lateral part of the petrous portion of the temporal bone contains the middle ear and the labyrinth. The more mesial portion constitutes the tip or apex. Within this tip is to be seen the internal carotid artery, which is separated from the overlying gasserian ganglion on the anterior surface of the petrosa by a thin plate of bone, which may be absent and replaced by fibrous tissue.

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1. Gradenigo, Guiseppe: Ueber circumscripte Leptomeningitis mit spinalen Symptomen und über Paralyse des Nervus abducens otitischen Uhrsprungs, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **62**:255, 1904.

The Trigeminus Nerve.—The relationship of this nerve to the petrous portion of the temporal bone is of the utmost importance in understanding the symptomatology of the lesion. The fifth nerve, both the motor and the sensory roots, after arising from the pons, passes forward and reaches the superior border of the petrous bone through an oval opening in the dura, above the internal auditory meatus. It then runs between the bone and the dura, along the superior surface of the petrosa, to the apex of the pyramid, where it terminates in the gasserian ganglion. This ganglion lies in a depression on the upper

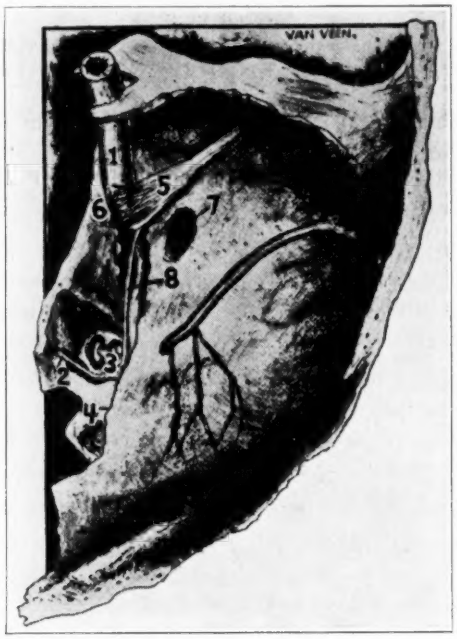

Fig. 1.—Photograph of the temporal bone viewed from above, with the gasserian ganglion lifted aside and the bony carotid canal opened (from Kopetzky and Almour). The cochlea and the superior semicircular canal are exposed. *1* is the carotid artery, *2* the facial nerve, *3* the cochlea, *4* the superior semicircular canal, *5* the gasserian ganglion, *6* the pyramidal tip, *7* the foramen ovale and *8* the great superficial petrosal nerve.

surface of the petrous apex, which, with the overlying dura to which the ganglion is firmly adherent, forms a pocket for its reception. Underneath the ganglion lies the great superficial petrosal nerve. From the ganglion three large branches are given off—the ophthalmic, the superior maxillary and the inferior maxillary nerve (fig. 1).

The ophthalmic branch deserves special consideration. Within the cavum mecklii the ophthalmic branch has a longer course than the

other two divisions. In this area it is firmly bound down and can be separated only with difficulty from the overlying dura and from the superior surface of the petrosa to which it is attached. In addition it is closely adherent to the cavernous sinus. The second and third branches of the fifth nerve, on the other hand, are not bound down in their course. In the ganglion the fibers rest on the carotid artery and the branches are not adherent to the dura. Consequently, any disturbance of the position of the gasserian ganglion will cause tension to be exerted on the ophthalmic division first, while the other two branches, because of their flexibility, can accommodate themselves for a time to their new position (Eagleton [2]).

The Abducens Nerve.—Dissections of this nerve by Dorello,[3] Vail,[4] and Wheeler [5] and lately by Eagleton [2] have given an accurate idea of its relationship to the petrous portion of the temporal bone. After leaving the lower border of the pons, the nerve runs upward and outward to pierce the dura over the sphenoid bone. It then turns forward and passes between the apex of the petrous bone and the posterior clinoid process of the sphenoid bone. The space between these two bony structures is formed into a canal by the interposition of a strong fibrous bundle, known as Gruber's ligament, or the petrosphenoid ligament. This ligament forms with the upper margin of the petrous bone a three-cornered space, termed Dorello's canal, and here lie the superior petrosal sinus and the abducens nerve.

Other Neurologic Structures.—Important structures include the facial nerve, the petrosal nerves and the three nerves in the jugular foramen (fig. 2). It is important to bear in mind that in its intratemporal course the facial nerve traverses both the petrous and the mastoid portion of the temporal bone. The great superficial petrosal nerve, arising from the facial nerve, and the deep petrosal nerve, arising from the carotid plexus, travel in grooves on the superior surface of the petrosa. They join and form the vidian nerve, which with the sphenopalatine branch of the second division of the trigeminus nerve forms the sphenopalatine ganglion. The small superficial petrosal nerve arises from the glossopharyngeal nerve (by way of the tympanic plexus and the tympanic nerve, of which it is a branch) and runs through the

2. Eagleton, W. P.: Localized Bulbar Cisterna (Pontile) Meningitis, Facial Pain and Sixth Nerve Paralysis and Their Relation to Caries of the Petrous Apex, Arch. Surg. **20**:386 (March) 1930.

3. Dorello: Ueber die Ursache der transitärischen Abduzenslähmung bei Mittelohreiterungen, Internat. Centralbl. f. Ohrenh. **4**:418, 1906.

4. Vail, H. H.: Anatomical Studies of Dorello's Canal, Laryngoscope **32**: 569, 1922.

5. Wheeler, J. M.: Paralysis of Sixth Cranial Nerve Associated with Otitis Media, J. A. M. A. **71**:1718 (Nov. 23) 1918.

petrous bone to enter the otic ganglion, thus establishing a connection with the third division of the trigeminus nerve. It has been established that disease of the petrous portion of the temporal bone may give rise to pain in areas supplied by the two ganglia mentioned.

It is important to be familiar with the pneumatization of the various structures of the temporal bone for a better understanding of the pathogenesis and clinical course of petrositis. Wittmaack [6] has shown that the air cells in the mastoid are developed by invagination of epithelial elements from the middle ear and the cells in the petrosa by a similar invagination. One should remember not only that the mastoid and zygomatic portions of the temporal bone may become pneumatized but

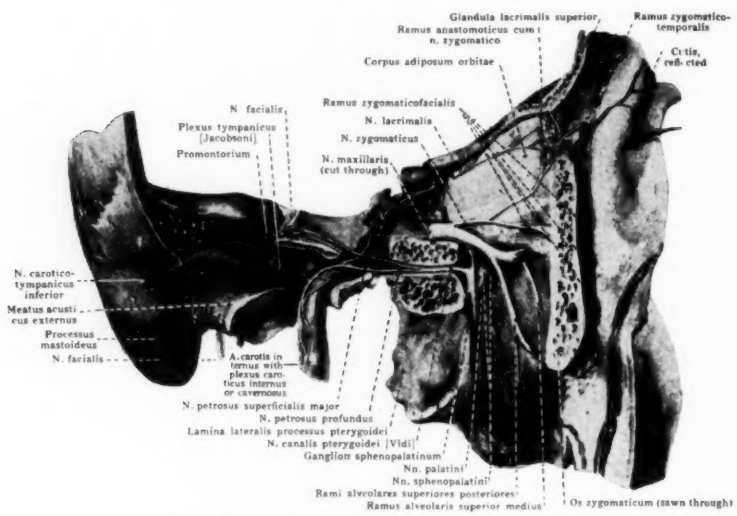

Fig. 2.—Photograph of the right vidian nerve, viewed from the right (from Spalteholz, K. W.: Hand Atlas of Human Anatomy, translation by L. F. Barker, Philadelphia, J. B. Lippincott Company, 1903, vol. 3, p. 692, fig. 766). The lateral wall of the orbit has been removed for the most part, and the pterygoid (vidian), carotid and facial canals and the tympanic cavity have been exposed.

that, as Kopetzky and Almour [7] have pointed out, in one third of all cases the temporal bone shows air cells in the petrous tip. The air cells communicate with one another and with the middle ear, so that if there is an inflammatory process in the middle ear there is a more or

6. Wittmaack, Karl: Ueber die Pneumatization des Schlafenbeines, Jena, Gustav Fischer, 1918.

7. Kopetzky, S. J., and Almour, R.: The Suppuration of the Petrous Pyramid: Pathology, Symptomatology and Surgical Treatment, Ann. Otol., Rhin. & Laryng. **40**:157 (March) 1931.

less inflammatory reaction in the mastoid and petrous cells; i. e., in every case of otitis media there is more or less mastoiditis, and if there are any cells in the petrosa, there is more or less petrositis. The more pneumatized the petrosa the more likely is involvement of this portion of the bone. However, there may be involvement of the petrous tip even when the spaces between the trabeculae of the bone are filled with marrow.

PATHOLOGIC CONSIDERATIONS

From a pathologic standpoint, the term petrositis (Fowler[8]) is differentiated as: (1) osteitis of the tip, i. e., inflammation of the bone separating the air cells of the pneumatized tip; (2) osteomyelitis of the tip, i. e., inflammation of the marrow and bone of the tip, and (3) osteitis or osteomyelitis of the perilabyrinthine regions.

Kopetzky and Almour,[7] after an exhaustive review of the literature and numerous personal observations, concluded that the avenues of infection to the pneumatized petrous tip are as follows: (*a*) from the antrum or epitympanic space, above or below the superior semicircular canal, along the posterosuperior surface of the petrosa into the pyramidal tip; (*b*) from the peritubal cells into the pyramidal tip, and (*c*) from the peritubal cells directly into the carotid canal, or through dehiscences in the anterior portion of the tympanic wall into the carotid canal and then rupturing into the cavum Mecklii.

These authors, after clinical observation of nine patients with suppuration of the petrosal tip, five of whom had recovered, drew the following conclusions regarding the pathogenesis of this disease:

1. All of our cases had an extensively pneumatized mastoid process. At the primary operation the cells extended well forward into the zygoma. In the region of the antrum and in the area posterior to the superior semicircular canal, cellular elements were present.

2. As the suppuration in the mastoid process and middle ear clears up, the suppurative process spreads into the perilabyrinthine tracts toward the pyramid.

3. After a period during which the middle ear remains dry, there suddenly reappears a profuse aural discharge, as a source of which the mastoid wound can be definitely ruled out, for it appears healthy and contains no pus. This finding leads us to believe with Lange that the pus within the petrous pyramid finds an avenue of escape by rupturing through the cells around the eustachian tube and then out through the middle ear.

These authors, like Fowler[8] and others, concluded that inadequate drainage of the petrosa may result in a chronic discharge from the ear even after the mastoid and the middle ear have been thoroughly cleaned.

Osteomyelitis of the petrosal tip is less common than osteitis and from a pathologic standpoint appears to have received less attention in

8. Fowler, E. P.: Suppuration of Petrous Tip, J. A. M. A. **102**:1651 (May 19) 1934.

the literature. In four of the seven cases in our series the condition occurred in pneumatized bone, and in three, in cancellous bone. In both cases in which there was a fatal outcome (cases 1 and 2) the lesion occurred in cancellous bone, as verified at autopsy.

The pathologic outcome of petrositis of the tip may be summarized as follows: (1) In some cases the condition recovers spontaneously or after simple mastoidectomy. This is more likely to occur when the tip is cancellous than when it is pneumatized (Eagleton [9]). Such was the outcome in five cases in our series. (2) The process may result in a fistula and become a cause of chronic otorrhea. (3) It may terminate in meningitis or brain abscess, either by perforation or by thrombophlebitis. (4) It may result in a retropharyngeal abscess (Greenfield [10] and Kopetzky and Almour [11]). (5) In some cases the course may end in recovery after surgical intervention.

SYMPTOMATOLOGY

Petrositis occurs much more commonly in association with acute than with chronic tympanomastoid infections. Thus, Kopetzky and Almour [12] reported only five of twenty-seven cases occurring in the course of chronic tympanomastoid disease, and Friesner and Druss,[13] two of nineteen cases. In three of seven cases in our series petrositis was chronic. Kopetzky [14] stated: "These (chronic forms) do not present a prodrome of meningitis. Nature has taken a hand in providing an egress for the pus accumulated in the petrosal pyramid." The symptomatology is therefore better known in the acute form, an outline of which follows:

It appears from the literature that osteitis of the petrous tip is far more common than osteomyelitis; it certainly has received a great

9. Eagleton, W. P.: Meningitis—Result of Disease of Petrous Apex and Sphenoidal Basis, Surg., Gynec. & Obst. **60**:586, 1935.

10. Greenfield, S. D.: Conservative Treatment of Petrositis: Report of Two Cases with Recovery Without Operation, Arch. Otolaryng. **20**:172 (Aug.) 1934.

11. Kopetzky, S. J., and Almour, R.: Report of Ten Cases of Suppuration in the Petrous Pyramid, Ann. Otol., Rhin. & Laryng. **44**:59, 1935.

12. Kopetzky, S. J., and Almour, R.: Empyema of the Petrous Apex: Further Observations and Case Reports, Ann. Otol, Rhin. & Laryng. **42**:802, 1933; footnotes 7 and 11.

13. Friesner, I., and Druss, J. G.: Osteitis of the Petrous Pyramid of the Temporal Bone Associated with Paralysis of the External Rectus, Arch. Otolaryng. **12**:342 (Sept.) 1930; Intracranial Complications of Otitic Origin, ibid. **15**:356 (March) 1932.

14. Kopetzky, Samuel: Problems Concerned with Empyema of the Petrous Apex, Arch. Otolaryng. **18**:47 (July) 1933.

deal more consideration than the latter. Kopetzky and Almour [7] divided the course of osteitis into four periods: the period of pain in the eye and aural discharge; the period of low grade sepsis; the period of quiescence, and the terminal stage. According to these authors, a typical course runs as follows: After a period of normal convalescence from mastoidectomy following an infection of the middle ear, during which the temperature returns to normal, the middle ear ceases to discharge; the mastoid wound heals normally, and the patient begins to complain of pain in the eye on the side of the lesion. About the same time there occurs a sudden profuse discharge from the middle ear but none from the mastoid wound, which by this time may have almost healed. The patient begins to have a low grade fever—99 F. in the morning and from 101 to 102 F. in the afternoon. The complaint of pain in the eye is made most frequently at night; at times the patient has a sensation of dizziness, with occasional vomiting. Transient facial palsy may be present. Examination at this time reveals profuse otorrhea, with discharge through a central perforation in the drum. There is slight nystagmus, which has no fixed direction. The fundi are normal. The blood count shows only moderate leukocytosis, with a slight increase in the number of staff cells. A roentgenogram of the petrous pyramid reveals distinct pathologic changes. If operation is performed at this time and the pus evacuated from the petrosa, recovery may ensue. If the lesion is permitted to advance, the pain in the eye subsides and disappears for a time. The patient feels well, and only the fever remains. After a short time, usually not exceeding ten days, fatal meningitis supervenes.

The preceding sequence and the rather sharp division into periods is questioned by some authors (Sunde [15]). It is also probable that in the average case and with every available method it may be difficult to differentiate osteitis from osteomyelitis, and in cases of the latter condition the course may not be so typical.

As in other intracranial complications of otitic origin, the neurologist, when confronted with possible petrositis, should observe and evaluate the following factors: [16] (*a*) chronological development of all symptoms and signs; (*b*) evidences of sepsis; (*c*) aural discharge, pathologic changes at operation and subsequent condition of the operative wound, and (*d*) results of roentgenographic studies.

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15. Sunde, E. A.: Infection of the Petrous Bone: Rationale of Treatment and Report of a Case, Arch. Otolaryng. **19**:346 (April) 1934.

16. Yaskin, J. C.: The Neurological Aspects of Intracranial Complications of the Ear and the Accessory Sinuses of the Nose, M. Times & Long Island M. J. **63**:305 (Oct.) 1935.

NEUROLOGIC MANIFESTATIONS

Ocular Pain.—There is general agreement that the ocular pain is fairly constant. Always homolateral and usually the first symptom, it is described as deep seated, within and behind the eye, and is generally worse at night. The pain sometimes radiates to the temporofrontal regions. This is the result of irritation of the ophthalmic division of the trigeminus nerve, which is firmly bound down in its course from the gasserian ganglion to and through the cavernous sinus. The irritation is caused by the inflammatory reaction of the dura overlying the diseased petrous tip and the petrosphenoid articulation (Eagleton [2]).

Ocular pain may appear early, coincident with the development of infection in the middle ear and mastoid, as in cases 2, 3 and 4 in our series. However, in the majority of cases reported the pain develops after operation, and a varying interval elapses between the performance of simple mastoidectomy and the appearance of ocular pain. In case 5 it developed only one day after operation, and in case 1, three and one-half months after the first operation. It was absent in cases 6 and 7.

From a neurologic standpoint, pain about the head and face occurring in the course of infection of the middle ear and mastoid, and especially after mastoidectomy, may be due to several causes, which should be carefully differentiated: (*a*) ordinary postoperative pain; (*b*) pain due to disease of the accessory nasal sinuses; (*c*) pain due to thrombosis of the lateral sinus—a dull, aching pain on the side of the head and accompanied by evidences of systemic infection; (*d*) nuchal pain characteristic of impending meningitis, and (*e*) pain due to involvement of the other branches of the fifth nerve from widespread inflammatory reaction in the external portion of the petrosa and the mastoid. Pain due to the last cause will be felt all along the area supplied by the second and third branches. This pain is not diagnostic, however, as it may be associated with uncomplicated abscess of the middle ear and mastoiditis. Any irritation of the geniculate ganglion of the facial nerve may cause pain to be referred to the area supplied by the superior maxillary branch of the trigeminus nerve. This occurs through the communication established between the geniculate ganglion and the second trigeminal branch through the great superficial petrosal nerve. The mandibular branch of the fifth nerve, through its connection with the otic ganglion, receives sensory fibers from the small superficial petrosal nerve. This may be irritated either at its origin in the tympanic plexus or in its passage through the petrosa to reach the otic ganglion. Irritation of Jacobson's nerve or the tympanic plexus may cause pain to be referred along the distribution of the superior maxillary nerve through

the great deep petrosal nerve, which joins the great superficial petrosal nerve.

It is clear, therefore, that pain in the face and teeth may occur in association with a suppurative lesion located anywhere in the middle ear or the mastoid process. This pain will be relieved, however, as soon as the source of irritation in the middle ear or mastoid is removed. Pain felt in the region of the orbit, due to irritation of the ophthalmic branch of the fifth nerve, is in all probability caused by a lesion in direct proximity to this branch, for it has no connection with the other sensory nerves in the petrosa.

When surgical removal of the purulent focus in the mastoid process and middle ear does not result in cessation of the pain distributed over the areas supplied by the second and third branches of the fifth nerve, persistence of the pain should be viewed as suspicious evidence of suppuration of the petrosal tip, when it is continuous and not spasmodic. Spasmodic pain is more likely to be associated with an idiopathic lesion of the gasserian ganglion, such as tic douloureux or neuritis. In cases of suppuration of the petrosal tip one is more likely to find a constant ache than a spasmodic pain.

Paralysis of the Abducens Nerve.—Paralysis of the homolateral abducens nerve in the course of petrositis is common but by no means constant. Reference may be made to some of the reported series of cases: Kopetzky and Almour [12] reported five cases in a series of twenty-seven; Friesner and Druss,[13] sixteen in a series of seventeen, and Eagleton,[2] three in a series of six. Smith [17] observed paralysis of the right nerve in all four cases in his series; Bowers,[18] in neither of his two cases; Roberts,[19] in three of four cases, and Bulson,[20] in each of his two cases. In our group of seven cases abducens palsy was shown in cases 1 and 20.

The causes of abducens paralysis in the course of petrositis are of interest to the neurologist. Dorello,[3] Vail,[4] Wheeler,[5] Eagleton [2] Sjöberg [21] and others have contributed much to an understanding of this condition. Eagleton's [2] dissections have shown that a number of factors influence the susceptibility of this nerve to lesions in the vicinity of the petrous apex which might disturb its functions. The difference

17. Smith, C. H.: Infections of the Petrous Pyramid, West Virginia M. J. **28**:7 (Jan.) 1932.

18. Bowers, W. C.: Two Cases of Petrous Bone Abscess Drainage: Recovery, Laryngoscope **38**:412, 1928.

19. Roberts, E. R.: Infection of Petrous Apex, Laryngoscope **44**:274, 1934.

20. Bulson, E. L.: Petrositis and a Consideration of the Gradenigo Syndrome, Tr. Indiana Acad. Ophth. & Otolaryng. **18**:84, 1934.

21. Sjöberg, A. A.: Contribution on the Knowledge of the Genesis of Certain Symptoms of Apicitis, Acta oto-laryng. **19**:479, 1934.

in the length of the nerve in Dorello's canal, the variation in the nerve itself and in its freedom in the canal and, especially, the structure of the bone itself help to determine whether or not the nerve will be involved in suppuration of the tip. A pneumatic bony structure, with cells extending from the middle ear to the petrous apex, is especially favorable for the development of abducens paralysis. These are the conditions in which recovery frequently follows simple mastoidectomy. The Dorello canal may vary on the two sides, and relative freedom on the affected side may be associated with contralateral abducens paralysis, due to a tight canal on that side.

Kopetzky and Almour [7] expressed the opinion that abducens paralysis is the exception rather than the rule and that its presence is more against than in favor of a diagnosis of suppuration of the petrosal tip. These authors stressed the importance of not waiting for the development of palsy of the external rectus muscle in arriving at a diagnosis of petrositis.

Abducens paralysis may appear at varying periods and in a number of conditions in association with infection of the temporal bone. Johnson [22] reported three cases in which abducens nerve palsy appeared early, before mastoiditis had manifested itself. Simple mastoidectomy produced complete cure. Paralysis of the abducens nerve may appear after simple mastoidectomy in association with pain in the face unaccompanied by evidences of sepsis, significant roentgen ray findings or meningeal irritation (the Gradenigo syndrome). Kopetzky [23] stressed the fact that early paralysis of the abducens nerve is not significant in relation to petrosal infection and that its late appearance presages the commencement of meningeal inflammation. The last observation was fully borne out in the two instances (cases 1 and 2) in our series, in which there was a fatal outcome.

Among other causes of abducens palsy may be mentioned localized and generalized meningitis, infection of the sphenoid bone (Eagleton [2]), thrombophlebitis of the veins in the peritubal region, thrombosis of the inferior petrosal sinus (Greenfield [24]) and various toxic conditions. Perkins [25] collected ninety-five cases of palsy of the abducens nerve. The causes in thirty-three cases were enumerated as follows: sinus

22. Johnson, W. H.: Abducens Paralysis Complicating Otitis Media and Mastoiditis, Ann. Otol., Rhin. & Laryng. **43**:94, 1934.

23. Kopetzky, S. J.: Acute and Chronic Otitis Media, Sinus Thrombosis and Suppuration of the Petrous Pyramid, Arch. Otolaryng. **22**:336 (Sept.) 1935.

24. Greenfield, S. D.: Etiology and Pathology of Paralysis of the Abducens Nerve Associated with Sinus Thrombophlebitis, Arch. Otolaryng. **19**:336 (March) 1934.

25. Perkins, C. E.: Abducens Paralysis and Otitis Media Purulenta, Ann. Otol., Rhin. & Laryng. **19**:692, 1910.

thrombosis in two, meningitis in three, labyrinthitis in four, abscess of the posterior fossa in nine, abscess of the middle fossa in two and petrositis in thirteen cases.

Involvement of Other Cranial Nerves.—Disturbances of these nerves result not from disease of the petrous tip but from lesions in the more external portions of the temporal bone, the middle ear, the labyrinth, the mastoid and the jugular foramen.

Facial weakness is infranuclear in type and is transient. Kopetzky and Almour [7] observed this in two of nine cases, and Friesner and Druss,[13] in three of nineteen cases. In the two cases reported by Kopetzky and Almour [7] there were also vertigo and nystagmus, which were ascribed to perilabyrinthitis. Vomiting may also be related to the same cause, or it may be of toxic origin. Nystagmus and vomiting were noted only in case 1 in our series. Involvement of the ninth, the tenth and the eleventh nerve indicates a grave intracranial extension.

EVIDENCES OF SEPSIS

The only important evidence of sepsis is low grade fever. In cases of petrositis the temperature ranges from 99 to 100 F. in the morning and from 101 to 102 F. in the afternoon. Low grade fever was present in five of our cases (cases 1, 2, 3, 4 and 7). When no other cause can be found for continued postoperative fever and when this is accompanied by pain in the eye and otorrhea, petrositis becomes a likelihood (Eagleton [2] and Kopetzky and Almour [7]).

The blood picture usually shows slight secondary anemia and moderate leukocytosis (with a count from 10,000 to 13,000). The invading organism, as obtained from the middle ear or the mastoidectomy wound, seems to have no specific etiologic relationship to petrositis. Spinal fluid studies yield no positive findings. The fever and all laboratory findings show marked changes with the development of meningitis.

AURAL DISCHARGE, OPERATIVE OBSERVATIONS AND CONDITION OF THE WOUND

Otologists agree that after well performed simple mastoidectomy has established adequate postauricular drainage, the middle ear should cease to discharge in a week or two. Continuation or recurrence of the aural discharge may be due to acute necrotic otitis, such as may occur in the course of scarlet fever or diabetes, to a secondary cholesteatoma or to petrositis of the tip (Kopetzky and Almour [7]). In the last-mentioned condition the aural discharge either continues or, after a period during which the ear is dry, reappears and is accompanied immediately or shortly afterward by pain behind the eye. In rare cases the pus may reopen an already healed mastoidectomy wound. The recurrence of otorrhea depends on the discharge of pus by way of the peritubal cells

or other channels created during the invasion of the petrous tip. At a secondary operation the mastoid region is observed to be clean; the middle ear and antrum are covered with granulation tissue, and in some cases fistulous tracts are seen leading to the petrous tip. These conditions may account for chronic otorrhea in some cases.

ROENTGENOGRAPHIC EXAMINATION

Roentgenographic examination is of inestimable value as an aid in establishing the diagnosis of petrositis. The importance of this procedure has been emphasized in contributions by Taylor [26] and Geyman and Clark.[27] As advocated by Taylor, we have made a roentgenogram showing a basal view of the skull as a part of our routine in every examination of the mastoid. This film is used for comparison with those taken at subsequent examinations should petrositis occur or be suspected. Since in the basal view both petrous pyramids are visible at the same time, this exposure presents the advantage of permitting a comparison of the side on which the lesion is suspected with the healing side. Contrary to the opinion of others, we have found the use of the Potter-Bucky diaphragm distinctly advantageous, since it greatly increases the clarity of the bone structure.

The basal view is of particular value in cases of suppuration of the petrous apex. However, in cases in which osseous destruction occurs in the base of the petrous pyramid and shows a tendency to invade the intracranial cavity by way of the petrous ridge, we have found the anteroposterior oblique projection of the pyramid more valuable. In cases in which petrositis is suspected, we also employ the Stenvers position.

In any of the three views mentioned it is possible to determine the presence and extent of pneumatization of the petrous pyramid, including the apex. From a clinical point of view the occurrence of petrosal pneumatization is extremely important, as infection from the middle ear or mastoid may spread more readily in a pyramid of this type than in a diploic pyramid.

In the roentgen interpretation of changes in the petrous pyramid the same criteria are employed as for the detection of pathologic changes in the mastoid. Almost invariably, as an accompaniment of acute otitis media or mastoiditis, there is noted increased density or clouding of the petrous pyramid. In many instances this represents congestive petrositis (cases 4 to 7) and is comparable with the congestive mastoiditis nearly always found in association with acute disease of the middle ear. This

26. Taylor, H. K.: The Roentgen Findings in Suppuration of the Petrous Apex, Ann. Otol., Rhin. & Laryng. **40**:367, 1931.

27. Geyman, M. J., and Clark, D. M.: The Roentgen Demonstration of Petrositis, Acta radiol. **13**:125, 1932.

occurs regardless of whether the petrosa is pneumatized or not. It is often difficult to recognize whether this appearance is due to edema of the surrounding soft parts or to actual congestive changes in the bone. The former can often be recognized by the fact that the density due to edema is not confined to the petrosa.

Congestive petrositis is usually not accompanied by clinical manifestations, and when it shows no evidence of progression, it is of no

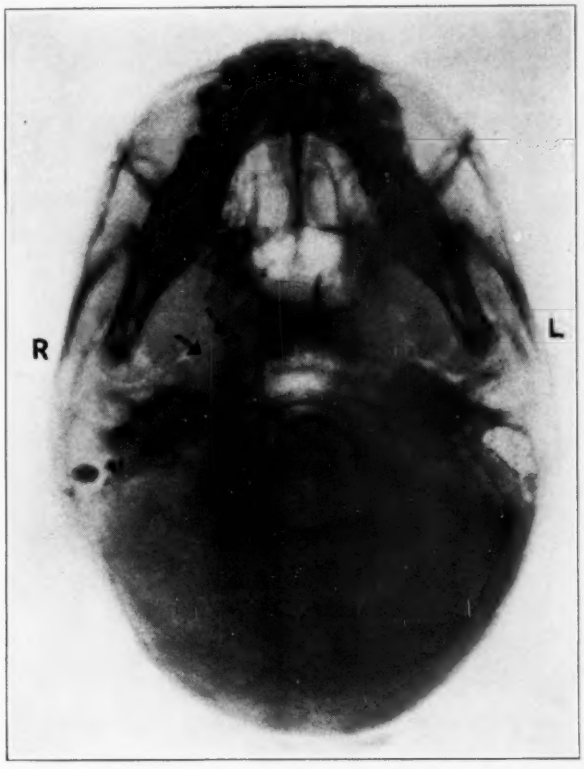

Fig. 3.—Roentgenogram of the basal view of the skull, showing a decrease in density indicating suppuration in the petrous apex on the right side, as compared with the normal appearance on the left.

more clinical significance than congestive mastoiditis. From the roentgenologic point of view, however, it is desirable to have a roentgenogram of the petrosa at this time, since it serves as a guide for comparison in the next stage of the disease, when, as the result of destruction of the bone, there are decrease in density and loss of bony detail, the involved area taking on a homogeneous appearance. This appearance usually implies suppuration and is characteristically seen in the petrous apex when that structure is pneumatized (fig. 3).

Suppurative petrositis in a diploic petrosa may present the moth-eaten or sievelike appearance which is characteristic of osteomyelitis in other portions of the skull. In seeking the path of least resistance, the osteomyelitis may break through the superior surface of the petrosa, invading the intracranial cavity. This occurrence is in most instances readily detected in the roentgenogram by a break in the continuity of the petrous ridge, as seen either in the anteroposterior oblique projection or in the Stenvers position (fig. 4).

Petrositis is far more commonly seen roentgenologically than clinically, if one includes the congestive variety of the disease. That this

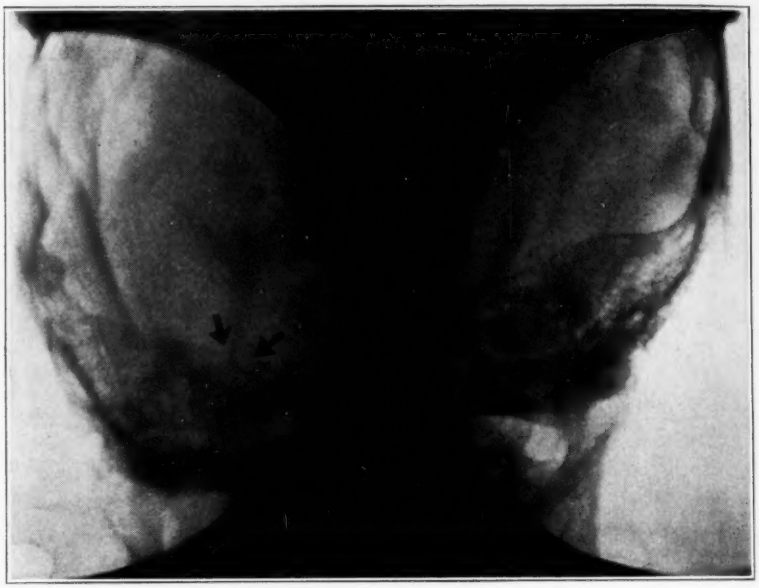

Fig. 4.—Roentgenograms showing osteomyelitis of the petrosa on the left side, causing dehiscence in the superior ridge of the petrous pyramid.

is true is verified by the frequency with which sclerotic changes are observed in one or both petrous pyramids in examination of the head made for causes unassociated with disease of the mastoid. That such changes are due to former petrositis is apparent by the evidence of old mastoiditis on the affected side. This is often the case in patients from whom no history can be obtained of previous mastoid trouble. From roentgen observation it is evident that mastoiditis, with its accompanying petrositis, frequently occurs without symptoms of sufficient severity to warrant a diagnosis of otitis media and that in such cases recovery, with or without surgical or spontaneous rupture of the ear drum, is the rule.

To the roentgenologist these preexisting attacks of mastoiditis and petrositis are of more than academic interest. The superimposition of acute infection is so often masked by the changes due to the preceding inflammatory process as to make destructive changes of recent origin almost impossible to detect. The roentgen examination is distinctly less valuable in a case of this type, and the clinician must place more reliance on clinical findings.

We are not entirely in accord with the statements in the literature that a roentgenographic diagnosis of petrositis should not be made in the absence of clinical symptoms. When the roentgen findings suggest petrositis, we believe that this fact should be brought to the attention of the clinician. Such a report should cause him to look more carefully into the clinical manifestations, since symptoms may have escaped his attention which on more careful examination can be detected. When the condition is at all suspicious, neurologic consultation should be sought. We do not believe, however, that therapy should be based on the roentgen findings alone, a statement which holds for practically all conditions in which roentgenography is used as a diagnostic procedure. It cannot be too strongly emphasized that the roentgen examination is of value only when correlated with the clinical aspects of the case.

DIAGNOSIS AND TREATMENT

The diagnosis of petrositis depends on the careful chronological evaluation of all the clinical data, but especially on the presence of (*a*) intra-ocular and retro-ocular pain and (*b*) evidences of low grade sepsis and continued or recurrent aural discharge not explained in any other manner, and possibly on the presence of (*c*) palsy of the abducens nerve and (*d*) positive roentgen findings. Kopetzky and Almour [11] stated:

> We feel that the lesion [petrositis] cannot be detected by roentgen findings only; nor can a diagnosis be considered authoritative upon clinical data alone. The two factors must be taken together. It is also necessary that all other factors which conceivably could cause the symptom complex must be checked and eliminated.

From a neurologic standpoint, the following conditions should be differentiated:

1. The Gradenigo syndrome. This syndrome appears to have lost its status as a clinical entity. Certainly, the occurrence of facial pain, paralysis of the abducens nerve and otorrhea is no longer as benign as was formerly regarded. In fact, it is likely that in not a few cases the so-called Gradenigo syndrome was petrositis and that in most instances of this syndrome in which the course ended in recovery the petrositis occurred in cancellous bone. The diagnosis of petrositis is not tenable when the facial pain is not characteristic (pain behind and in the eye),

when there is absence of evidence of sepsis and when repeated roentgenograms show normal structure.

2. Pain resulting from disease of the accessory nasal sinuses. Pain can be differentiated easily by clinical and roentgenographic studies.

3. Meningitis in the anterior fossa. Meningitis in this region may give rise to facial pain which occasionally resembles the unilateral supraorbital pain characteristic of petrositis. Studies of the spinal fluid will usually establish an accurate diagnosis.

4. Abscess of the temporosphenoid lobe. This may give rise to facial pain. The coexistence of homonymous cuts in the visual fields and the somewhat later evidences of increased intracranial pressure and other signs of focal involvement of the brain (aphasia in association with lesion of the left side in right-handed persons, and contralateral central facial palsy) may help in making a differential diagnosis.

5. Acute perilabyrinthitis and labyrinthitis. These conditions may be associated with pain in the face. The presence of vertigo and nystagmus, positive reactions to the Bárány test, which give negative results in cases of petrositis, and normal roentgen findings will help in establishing a diagnosis.

6. Thromboses of the lateral, cavernous and superior and inferior petrosal sinuses. Thrombosis of these sinuses may give rise to facial pain, and involvement of all but the lateral sinus, to paralysis of the abducens nerve. The evidences obtained by blood counts and blood cultures, the markedly septic course in the majority of cases and the normal roentgen findings help in the diagnosis. In thrombosis of the lateral sinus the information obtained by the Ayer-Tobey test and in thrombosis of the cavernous sinus, the proptosis and additional involvement of the third and fourth nerves are diagnostic.

The treatment of petrositis is not a neurologic or a neurosurgical problem. Adequate reviews have been made by Kopetzky and Almour,[12] Coates, Ersner and Myers [28] and others.

REPORT OF CASES

CASE 1.—*Acute mastoiditis following chronic recurrent infection of the right middle ear; simple mastoidectomy on Jan. 5, 1934. The ear remained dry only for a short time, and low grade fever continued until early in March, when the temperature became higher and there developed successively headache, vomiting, nystagmus, palsy of the right external rectus muscle and roentgenographic evidence of petrositis. Death occurred from meningitis. Autopsy showed osteomyelitis of the petrous tip.*

C. P., a girl aged 7 years, who had had chronic recurrent infection of the right middle ear for four years, in December 1933 contracted an infection of the

28. Coates, G. M.; Ersner, M. S., and Myers, D.: Roentgen Changes in the Petrous Portion of the Temporal Bone Without Clinical Manifestations, Arch. Otolaryng. **20**:615 (Nov.) 1934.

upper respiratory tract and acute mastoiditis on the right. A simple mastoidectomy was performed by Dr. S. Cohen at the Northern Liberties Hospital, Philadelphia, on January 5; the patient was discharged on January 23. A few days after her discharge from the hospital, the ear became dry, and the operative wound looked well, but she was kept in bed for three weeks because of daily elevation of temperature. The ear remained dry for only a few days, and then discharge recurred both from the ear and from the mastoidectomy wound. The temperature became more elevated. The child was readmitted to the hospital March 7, but there were no significant findings to account for the symptoms. She continued to have a rise in temperature (from 99 to 100 F. in the morning and 101 F. in the afternoon), and there was some aural discharge. On March 16 she complained of headache and on March 18 of pain in the right eye, and lateral nystagmus was noted. On March 19 complete palsy of the right external rectus muscle was noted. She vomited about once daily, was irritable and slept poorly. A roentgenogram of the petrous tip on March 13 showed no involvement. The patient was discharged on March 21, with only a slight rise of temperature in the afternoon and slight otorrhea.

Examination.—On March 25 the temperature varied from 99 to 104 F. There were no chills or sweats and only slight occasional headache. On the patient's admission to the Graduate Hospital (service of Dr. G. B. Wood) on March 20, the presenting symptoms were otorrhea on the right, diplopia and vomiting spells. The temperature was 102 F., the pulse rate 130 and the respiratory rate 30. The child appeared toxic, pale and apathetic. Somatic examination gave otherwise normal results. There was only a slight discharge from the right ear; the mastoidectomy wound looked healthy. Neurologic examination revealed anesthesia of the right cornea, complete paralysis of the right external rectus muscle and inconstant, nondirected lateral nystagmus. All other examinations gave normal results. The urine contained a trace of albumin and occasional granular casts. A blood count revealed: erythrocytes 4,490,000, hemoglobin 58 per cent, leukocytes 14,000 and polymorphonuclears 84 per cent.

Results of roentgen examination were as follows: The mastoids were large. Pneumatization was of the small and large cell variety, with cells extending into the squamous and zygomatic portions of the temporal bone. The sigmoid sinus was not well shown on either side; its anterior wall probably occupied a posterior position. The left mastoid was normal. The right mastoid showed loss of cell structure throughout most of the process. This was evidently due to previous operations. Probably some cells remained in the tip of the mastoid and the region of the antrum. Films made of the petrous pyramid showed a large defect in the superior surface, in the region of the cochlea. This was evidently due to suppuration, with extension into the intracranial cavity. The tip of the petrous pyramid was not pneumatized. The conclusion was: acute suppurative mastoiditis on the right side, with petrositis involving the base of the petrous pyramid and possible extension into the intracranial cavity.

Course.—On March 30 the right lateral sinus was exposed and observed to be essentially normal. The middle cranial fossa was exposed, and no collection of pus or other visible abnormality was seen. On March 31 a blood transfusion was made. The patient then began to show a Kernig sign, and in the succeeding few days meningitis developed. Studies of the spinal fluid revealed purulent meningitis, with gram-positive extracellar cocci. Repeated transfusions, lumbar taps and other palliative measures were carried out. The patient died on April 9.

Autopsy (Dr. E. Case).—Macroscopic Observations: On removal of the skull cap, the dura was seen to be adherent to the inner table, but separation was

easily effected. When the dura was removed, a fairly thick layer of yellow-greenish pus and fibrin was observed in the subarachnoid space, spread diffusely over the entire cerebral hemispheres and involving also the brain stem. The various venous sinuses were examined, with special attention to the lateral sinuses, but no thrombosis or frank pus was observed. The cerebellar surfaces were free from exudate. The surface of the petrous portion of the right temporal bone was devoid of a periosteal covering and was moth eaten and dull. On probing and removal of a fragment, the bone was seen to be friable, the interstices being filled with necrotic material and pus. The left petrous bone was intact. In the right mastoid region a recent operative wound was draining pus. The mastoid

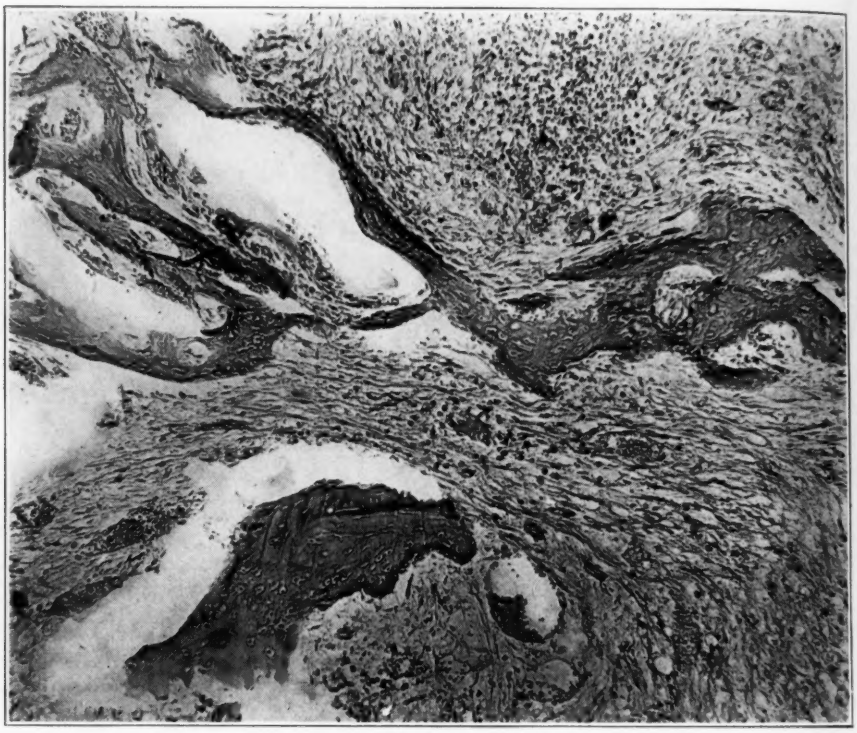

Fig. 5 (case 1).—Photomicrograph (low power) showing a diffuse fibrous and cellular reaction among the spicules of bone.

portion of the right temporal bone had been hollowed out by a recent mastoidectomy. On section of the brain nothing of pathologic significance was observed. Cultures of pus from the subarachnoid space were positive for Streptococcus haemolyticus.

The gross pathologic diagnosis was acute diffuse meningitis, and suppurative mastoiditis and petrositis (right side), with extension into the intracranial cavity.

Microscopic Observations: The petrous tip of the right temporal bone showed necrotic changes in various areas, mostly of the granular type. The bone marrow appeared normal except for slight cellular infiltration. There was necrosis of bone (figs. 5 and 6).

Brain: The pia was covered with a thick layer of inflammatory exudate, which also dipped into the sulci. The vessels were greatly congested and dilated. In one area the surface brain tissue showed marked granular degeneration and necrosis.

The patient had a chronic infection of the middle ear, which was followed by mastoiditis and osteomyelitis of the petrosal tip and terminated in meningitis. In this case the established symptoms were present: chronological development, evidences of sepsis, continued aural dis-

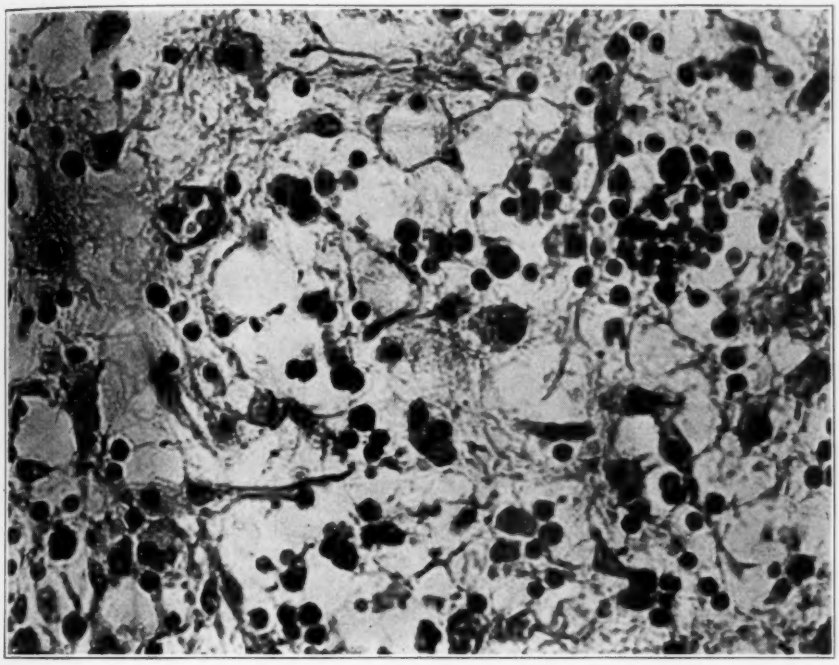

Fig. 6. (case 1).—Photomicrograph (high power) in which the nature of the cells is clearly seen. They are composed of large mononuclear cells, lymphocytes and occasional polymorphonuclear cells.

charge, ocular pain, paralysis of the abducens nerve, nystagmus and vomiting and positive roentgen findings.

CASE 2.—*A boy had a cold in December 1934, which was associated with transient diplopia; in January 1935 nocturnal pain in the left ear and on February 4 pain in the left ear and on the left side of the head, with acute mastoiditis and bulging, but not perforation of the ear drum. Simple mastoidectomy on February 5 was followed by low grade fever and eight days later by pain in the left eye, paralysis of the left abducens nerve and fatal meningitis. Autopsy revealed necrosis of the left petrous tip.*

L. G., a boy aged 8 years, was admitted to the Graduate Hospital (service of Dr. W. Roberts) on February 4, complaining of pain in the left ear and the left

side of the head. In the latter part of December 1934 he had had a cold, which did not confine him to bed. About Christmas 1934 he complained of diplopia. In the first week in January 1935 the cold disappeared but he had pain in the left ear, which was inconstant and worse at night. There was no aural discharge, and the ear was treated with irrigation and drops.

Examination.—On his admission to the hospital the temperature was 100 F., the pulse rate 110 and the respiratory rate 22. The boy was poorly developed and poorly nourished. Coarse râles were heard in the chest posteriorly. The left ear drum was bulging, but there were no perforations or aural discharge. There was exquisite tenderness over the left mastoid and the adjacent occipital region. There was cervical adenopathy bilaterally. Neurologic examination gave normal results. The urine was normal. A blood count showed: erythrocytes 4,160,000, hemoglobin 55 per cent, leukocytes 11,800 and polymorphonuclears 79 per cent.

Results of roentgen examination on February 4 were as follows: the mastoids were unusually large. Pneumatization was of the small and large cell variety, with cells extending into the squamous and zygomatic portions of the temporal bone. The anterior wall of the sigmoid sinus occupied a midposition. The right mastoid was normal. The left mastoid was unusually clear but showed definite thinning and destruction of many cell walls, particularly over the sigmoid sinus. The conclusion was: The appearance was that of acute coalescent suppurative mastoiditis.

Course.—On February 5 a simple mastoidectomy was performed. Pus was uncovered by removal of the cortex. Many cells posterior to the lateral sinus plate were removed. The lateral sinus was not explored. The patient complained of pain in the right eye, but the temperature dropped to normal. From February 6 to 13 he had low grade fever (the temperature ranging from normal in the morning to about 100 F. in the evening) and was irritable. He occasionally complained of pain in the mastoid region. On February 13 he began to complain of pain in the left eye and of double vision. The temperature was elevated to 101 F. and was sustained. On February 14 there were rigidity of the neck, bilateral Kernig sign, paralysis of the left external rectus muscle and anesthesia of the left side of the face, which was more marked in the distribution of the lower two divisions of the fifth nerve. Lumbar tap revealed normal pressure (120 mm. of water), a clear fluid, and a cell count of 20 per cubic millimeter. The smear contained no organisms. A blood count showed 17,400 white cells, with 82 per cent neutrophils. Roentgen examination was reported as follows: The right mastoid was normal. The left mastoid showed an operative defect resulting from the recent mastoidectomy. There was a rather clear area of dehiscence in the petrous pyramid just anterior to the eminentia arcuata. This looked like an area of bone necrosis, and because of this finding, which was not present in the preceding films, we were inclined to regard osteomyelitis of the petrous bone as a possibility. Involvement of the bone did not extend into the apex of the petrous pyramid, which made us think that the infection of the petrous pyramid was of the Eagleton type rather than that described by Kopetzky and Almour. The conclusion was: osteomyelitis of the petrous bone (fig. 4).

On February 15 the temperature was from 103 to 105 F.; meningeal signs were marked, and the spinal fluid showed a marked increase in the number of cells, from which a nonhemolytic streptococcus was recovered. The lateral sinus and the middle and posterior cranial fossae were exposed, and further curettement in the direction of the petrous tip was carried out. In the succeeding few days meningeal signs increased; sugar disappeared from and the chlorides were reduced

(280 mg.) in the spinal fluid. The Kubie treatment was started on February 17 but proved of little value. Death occurred on February 20.

Autopsy (Dr. E. Case).—Macroscopic Observations: A surgical wound, with the edges ragged and separated, occupied a position over the left mastoid area. The mastoid cells in that region had been removed and the dura exposed. On opening the skull, the vessels of the cerebrum showed considerable congestion. A yellowish green, purulent exudate had collected in the subarachnoid space in the left temporal region and over the entire base of the brain, with extension into the right temporal lobe. Pus was also seen in smaller amounts along the course of the cerebral vessels, near the base of the brain. The left lateral sinus contained an organized thrombus, which extended for a short distance into the sigmoid portion. The tip of the petrous portion of the left temporal bone was necrotic, with much of the bone replaced by hemorrhagic purulent exudate. Sloughing of the bone occurred in the immediate vicinity of the ganglion of the fifth nerve, and by this route the infection probably had gained entrance to the meninges. The mastoid and petrous portions of the temporal bone were removed in toto. On sectioning the brain, the purulent exudate was observed to be confined to the meninges. No area of softening or abscess formation was present in the brain tissue.

The gross pathologic diagnosis was mastoidectomy on the left side; diffuse purulent meningitis; thrombosis of the left lateral sinus and necrosis of the petrous portion, including the tip, of the left temporal bone.

Microscopic Observations: Sections were removed from areas where gross accumulation of purulent exudate occurred in the overlying pia-arachnoid covering. A thick inflammatory exudate was seen, consisting mostly of polymorphonuclear leukocytes, round cells, fibrin and plasma cells. Large phagocytic cells were present in abundance. This exudate occupied the pia-arachnoid spaces and followed the pia as it dipped into the sulci. The brain tissue immediately underlying the pia showed a slight degree of destruction and inflammatory cellular infiltration, resulting from direct extension.

The diagnosis was diffuse purulent leptomeningitis. Sections of bone in the region of the petrous tip showed evidences of osteomyelitis, similar to those in case 1 (figs. 5 and 6).

In this case the infection of the middle ear spread both to the mastoid and to the petrosa, causing osteomyelitis of the tip and meningitis. Transient diplopia antedated any aural symptoms, and there was no spontaneous perforation of the drum. Evidences of sepsis, however, existed from the start, and ocular pain and abducens palsy were late symptoms. Roentgen evidences of petrositis did not develop until after simple mastoidectomy was performed.

CASE 3.—*Discharge from the ear, accompanied by low grade fever; evidences of sepsis; ocular pain for two months, and roentgen evidences of mastoiditis. A first mastoidectomy gave no relief, and a second roentgenogram revealed the existence of petrositis. A second mastoidectomy resulted in complete recovery.*

A. G., a boy aged 14 years, was admitted to the Graduate Hospital (service of Dr. W. Roberts) on April 6, 1936, complaining of a discharge from the right ear and recurrent pain in the right eye. The family and the past medical history were irrelevant. About two months prior to his admission to the hospital the boy sustained wounds over his body as the result of a chemical explosion, and at

about the same time there developed a cold which was followed by spontaneous discharge from the right ear. Since, in addition to the discharge from the ear, he had had low grade fever and recurrent pain within and behind the right eye. He lost about 10 pounds (4.5 Kg.) in weight and had not attended school for two months.

Examination.—The general physical examination was essentially normal. Examination of the right ear revealed a white discharge, impairment of hearing, perforation of the ear drum and no tenderness of the mastoid. Neurologic examination gave normal results. A blood count showed: erythrocytes 4,480,000, hemoglobin 75 per cent and leukocytes 13,600, with 66 per cent polymorphonuclear cells. Urinalysis gave normal results. Spinal puncture was not performed. Roentgen examination on April 2 was reported as follows: Both mastoids were well pneumatized, the cells were chiefly of the small variety. The anterior wall of the sinus was not visualized in the left mastoid but was distinct in the right. The left mastoid revealed evidence of pathologic change. In the right mastoid the cell outlines were considerably blurred, although there did not seem to be acute destruction of the bony septums. The mastoid cells appeared to be filled with secretion, which was rather dense, possibly due to pus. The conclusion was: mastoiditis, possibly acute, involving the right mastoid, and no distinct evidence of destruction of the bony septums.

Course.—On April 10 paracentesis was done, and on April 18 a simple mastoidectomy was performed on the right. In spite of these procedures, the temperature varied from day to day, but there was generally an afternoon rise. The ear continued to discharge. The boy had recurrent pain in the right eye, and the leukocyte count remained high. On April 20 roentgenographic study revealed: The petrous bone on the right showed extensive destruction of the apex. This was present to some extent at the preceding examination but was much more marked at the second. The left petrous bone was completely pneumatized, cells extending from the mastoid to the petrous apex. As far as we were able to determine, the operative site in the right mastoid seemed to be in good condition. The conclusion was: evidence of extensive suppuration of the petrous apex on the right side (petrositis) (fig. 3).

On April 23 a second mastoidectomy was performed, and the middle fossa was explored. For the succeeding few days the temperature become normal, but pain in the right eye persisted until April 28. The patient was discharged on May 5, 1936, in good condition.

This case is typical of the group described by Kopetzky and Almour.[7] The second mastoidectomy apparently afforded more adequate drainage.

CASE 4.—*Clinical evidences of acute mastoiditis and roentgen evidence of acute mastoiditis and petrositis. Nine days after admission to the hospital the temperature fell, but discharge from the ear continued; in addition, there developed ocular pain. Simple mastoidectomy resulted in relief of all symptoms, but roentgen examination showed progression of pathologic changes in the petrous tip.*

S. S., a woman aged 28, was admitted to the Graduate Hospital (service of Dr. G. M. Coates) on March 9, 1935, complaining of pain in the right ear. Two weeks before the patient had had a severe cold. A week later pain began in the right ear. Myringotomy was performed twice. There were fever, backache, pains in the legs, malaise and symptoms of involvement of the upper respiratory tract. The general systemic symptoms subsided; pain and discharge from the right ear continued, however, and there was elevation of temperature.

Examination.—On admission to the hospital the patient's temperature was 100 F., and the pulse rate 110. General physical and neurologic examination gave normal results. The left ear was normal. The right ear drained pus, and there was tenderness over the mastoid. Urinalysis gave normal results. A blood count showed: erythrocytes 4,440,000, hemoglobin 67 per cent, leukocytes 9,200 and polymorphonuclears 82 per cent. Results of roentgen examination on March 12 were as follows: Both mastoids were well pneumatized, the pneumatization extending into the zygomatic region. The mastoid cells were of normal appearance on the left side. On the right there was evidence of destruction of the cells of the tip and the periantral region. On this side the sigmoid sinus was large and occupied a midposition. There was no evidence of involvement of the petrous pyramid. The conclusion was: suppurative mastoiditis on the right side.

Course.—The temperature fell to normal in two days and remained so. The ear continued to discharge, and there was occasional otalgia. On March 18 there developed considerable pain over the right frontal region unaccompanied by any rise in temperature. Examination of the sinuses gave normal results. However, the roentgen report on March 20 was: There apparently had been progression of the destructive process in the base of the right petrous pyramid since the last examination. The area of involvement was just beneath the tegmen. There was also at this time definite clouding of the petrous apex which was not present at the preceding examination. The petrous apex was pneumatized. We found no definite evidence of cellular destruction in this region. The conclusion was: definite evidence of progression of the destructive process in the right mastoid and extension toward the apex of the petrous pyramid.

On March 22 simple mastoidectomy revealed a few infected cells in the mastoid tip. At operation the inflammatory process appeared to be subsiding and the condition was much better than was indicated by the roentgenograms. A culture of the material from the mastoid field yielded a hemolytic streptococcus. The patient was discharged in good condition on April 4, 1935.

The only neurologic symptom in this case was the ocular pain. The petrous tip was not pneumatized, and the roentgen findings probably indicated congestion, which was relieved by appropriate and timely drainage.

CASE 5.—*Several weeks after acute otitis media there appeared clinical evidences of acute afebrile mastoiditis and roentgen evidences of acute mastoiditis and acute or chronic petrositis. Simple mastoidectomy was followed by transient ocular pain and afebrile reaction; complete clinical recovery was the end-result.*

L. G. a Negro aged 34, a laborer, in November 1933 had buzzing in both ears. Several hours later he experienced throbbing pain in the left ear. On the following day the left ear discharged blood-stained yellow pus. This terminated the pain temporarily. A week later the pain in the left ear recurred, and pain appeared in both sides of the neck posteriorly. This pain remained almost constant up to the time of the patient's admission to the Graduate Hospital (service of Dr. W. Roberts) on Feb. 1, 1934. In the preceding week, however, the pain had diminished, especially on the left side. With the pain in the neck the patient often experienced pain all over the head. The left ear had discharged since November. In the five days prior to admission the region just above the left ear had become swollen, and there was also pain in the left side of the jaw, which rendered opening the mouth painful. The patient thought he had had some stiffness in the neck with the nuchal pain. He had no other significant symptoms.

Examination.—On the patient's admission to the hospital the temperature and the pulse rate were normal. General physical and neurologic examinations gave normal results. There was a questionable lagging of the left side of the face. The left ear drum could not be visualized because of swelling of the wall of the canal. There were tenderness and swelling over the left emissary vein, the antrum and the zygomatic process. The right ear drum showed a perforation but no other abnormalities. Urinalysis gave normal results. A blood count on February 2 showed 13,400 leukocytes, 78 per cent polymorphonuclears, and 4,270,000 erythrocytes, with 72 per cent hemoglobin. The Wassermann reaction of the blood was negative. Spinal puncture was not performed. The sugar content of the blood was 91 mg. and the urea nitrogen content 12 mg. per hundred cubic centimeters. The roentgen report on February 2 was: The mastoids were large. Pneumatization was of the small and large cell variety, with cells extending into the squamous portion of the temporal bone. The sinus plate occupied a midposition. The right mastoid showed clouding throughout, with thickening of the cell walls. This was evidently the result of an old inflammatory process. On the left side there was marked clouding, with considerable indistinctness in cellular outline. The appearance was that of acute suppurative mastoiditis, with some cellular destruction. A basal view of the skull showed marked clouding of the entire petrous pyramid, including the apex on the left side. This denoted an inflammatory reaction, which might be a part of the acute process or the result of an old chronic infection. If the patient had no symptoms of petrositis, the appearance at the time of roentgenography may be regarded as the result of a preexisting inflammatory process. The petrous pyramid on the right side was well pneumatized. The conclusion was: acute, suppurative mastoiditis on the left side, with acute or chronic petrositis.

Course.—Simple mastoidectomy was performed on February 3. A considerable amount of pus was observed, but no fistula. The zygomatic cells were involved and were cleaned. On February 6 the patient had considerable discomfort behind the eyes, especially the left. This lasted for a few days, but he made a good surgical recovery and was discharged on February 12. A culture yielded nonhemolytic staphylococci (Staphylococcus aureus). Throughout his residence in the hospital there had been no rise in temperature except on February 6, when the ocular pain commenced; the temperature then was elevated to 100 F.

In this case and the next two cases the diagnosis of petrositis is based entirely on the roentgen findings. It is interesting, however, that after operation there was a febrile reaction, with transient ocular pain.

CASE 6.—*Discharge from the ears for twenty-one years and severe pain in the neck and temples for a few days. Roentgen examination revealed bilateral osteosclerosis and chronic petrositis on the left side. No objective neurologic symptoms. After radical mastoidectomy on the right side, the ear became dry. The discharge from the left ear continued. Pain disappeared.*

M. S., a Negress aged 23, was admitted to the Graduate Hospital (service of Dr. G. M. Coates) on July 16, 1934, complaining of pain in the head. Running from the ears developed after typhoid and malaria, at the age of 2 years. Since, there had been a regular discharge, with periodic pain confined to the ears. In 1933 "something broke, and blood and pus escaped from the right ear." On July 15, while preparing dinner, the patient had a severe stabbing pain, which started in the back of the neck and radiated across the head to both temporal regions. The pain lasted one or two minutes. She did not have a second attack of pain

until 9 p. m., on July 15. Since, the pain had been frequent, lasting from one to two minutes and being extremely severe. There was no vomiting or trauma. The patient said that she had no ocular symptoms. She had had her tonsils removed about a year before. Since, she had had a discharge from the right ear of a small amount of black, tenacious material, which occasionally was mixed with red blood. There never had been a copious quantity or any foulness.

Examination.—On the patient's admission to the hospital the temperature and pulse rate were normal, and they remained so throughout her residence in the hospital. General physical and neurologic examinations gave normal results. Both auditory canals were filled with a purulent discharge, more so on the right. The ear drums appeared sclerotic. There was no tenderness over either mastoid region. Bárány tests gave negative results. The patient was observed in an attack of pain, during which there was horizontal rotary nystagmus unaccompanied by vertigo or vomiting. Urinalysis, a blood count, a Wassermann test of the blood and spinal fluid studies gave normal results. The roentgen report on July 16 was: The mastoids were of average size. Most of the mastoid structure was diploic. There were markedly increased density on both sides and increased prominence of the anterior wall of the sigmoid sinus. The appearance was that of bilateral osteosclerosis the result of a preexisting suppurative process of long standing. We could not exclude active suppuration on either side. The left side appeared to be most involved. The film of the base of the skull showed what appeared to be destruction of bone in the region of the tip of the left petrous apex which suggested that the patient had had petrositis at some time. The conclusion was: bilateral osteosclerosis, the result of a chronic suppurative process, and evidence of preexisting petrositis on the left side.

Course.—Radical mastoidectomy was performed on the right side on July 27, after which the discharge on the right side disappeared; on the left side, on which mastoidectomy was not performed, the discharge continued. The patient was discharged on August 10 and up to the time of writing has had no intracranial complications.

The diagnosis of petrositis in this case was based entirely on roentgen examination. It was evident from the associated findings that the condition was of long standing. In the absence of symptoms the evidence of petrositis was of no clinical significance. A case of this type is not uncommon.

CASE 7.—*Clinical and roentgen evidences of acute mastoiditis. Simple mastoidectomy was followed by prompt and complete recovery, but subsequent roentgen studies revealed the development of petrositis.*

F. R., a girl aged 7 years, was admitted to the Graduate Hospital (service of Dr. E. B. Gleason) on Feb. 28, 1934, with elevation of temperature and discharge from the left ear. The child had had a cold a month prior to her admission and one week later had complained of otalgia on the left and discharge, by spontaneous perforation. The ear had discharged since.

Examination.—On admission the patient had a temperature of 101 F., with a pulse rate of 130. General physical examination revealed that the child was undernourished, pale and toxic. Neurologic examination gave normal results. The right ear was normal. The left auditory canal was filled with pus. There were redness, swelling and tenderness over the left mastoid region. The blood count on February 28 was: erythrocytes 3,640,000, with 43 per cent hemoglobin and leuko-

cytes 9,700, with 61 per cent polymorphonuclears. Results of roentgen examination on February 28 were as follows: The mastoids were fairly large, and pneumatization was of the small and large cell variety, with cells extending into the squamous and zygomatic portions of the temporal bone. The sinus plate occupied a posterior position. The right mastoid was normal. The left mastoid showed generalized clouding throughout. There was definite evidence of cellular destruction over the sigmoid sinus. The conclusion was: acute suppurative mastoiditis on the left side.

Course.—Simple mastoidectomy was performed on March 5. Pus was present over the vertical portion of the facial nerve and down to the lateral sinus. The sinus was normal in appearance and was uncovered for about 1 inch (2.54 cm.). The temperature dropped to normal within two days, and the child made a satisfactory recovery. However, a second roentgen study on March 5 was reported as follows: There appeared to have been further destruction of the cell walls of the left mastoid since the last examination. This was particularly marked over the sigmoid sinus and extended well down toward the tip of the mastoid. The film of the base of the skull showed definite clouding throughout the petrous pyramid, with obscuration of detail. This was evidently due to acute petrositis. The conclusion was: acute suppurative mastoiditis and acute petrositis on the left side. A blood count on March 19 showed: 4,160,000 erythrocytes, 58 per cent hemoglobin and 5,500 leukocytes, with 67 per cent polymorphonuclears. The child was discharged on March 22, in good condition.

This case is of interest because of the roentgenographic evidence of petrositis, in the absence of any clinical findings. It is generally recognized that the roentgen findings can be evaluated only in relation to other considerations.

SUMMARY

Petrositis, which has assumed considerable importance in recent years, occurs in two forms: as osteitis in pneumatized cells and as osteomyelitis in cancellous bone. Both forms occur mainly in acute conditions but also in chronic diseases of the middle ear and of the mastoid, and probably account for many intracranial complications of disease of the ear. The neurologic symptoms arising from petrositis depend on the relation of the pyramid to the gasserian ganglion and its branches, to the abducens nerve and to the petrosal nerves. The presenting symptoms include retro-ocular pain, less frequently paralysis of the abducens nerve, evidences of low grade sepsis and continued or recurrent aural discharge. Roentgen examination is an important part of the clinical investigation. Petrositis is to be differentiated from the more benign Gradenigo syndrome, meningitis of the anterior fossa, cerebral abscess, thrombosis of the venous sinuses, acute labyrinthitis and perilabyrinthitis and disease of the paranasal sinuses.

Seven cases are reported. In two instances acute petrositis was associated with acute mastoiditis and petrositis, and the diagnosis was verified at autopsy. In two cases of mastoiditis and petrositis the illness ended in recovery after simple mastoidectomy. In two other cases there

were acute mastoiditis and petrositis unaccompanied by any neurologic manifestations, followed by recovery after simple mastoidectomy. In the seventh case there was chronic bilateral mastoiditis, in which one side showed chronic petrositis but no neurologic symptoms. Three of the seven cases occurred in the course of chronic tympanomastoid infection. Ocular pain occurred in five cases and paralysis of the abducens nerve in two.

The prognosis in these cases depends on timely intervention, and the indications for surgical treatment should receive the critical attention of the otologist, the roentgenologist and the neurologist. The neurologist, when confronted with neurologic complications of otologic disease, not only should make a complete neurologic examination but should consider the chronological development of the symptoms, the systemic evidences of sepsis, the presence of an aural discharge, the observations at operation, the subsequent condition of the operative wounds and the results of roentgen studies.

CEREBRAL CIRCULATION

XLIV. VASODILATION IN THE PIA FOLLOWING STIMULATION OF THE VAGUS, AORTIC AND CAROTID SINUS NERVES

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Central stimulation of the vagus nerve in animals is followed, under certain conditions, by dilation of arteries in the pia-arachnoid. When first reported in 1928 this dilation was thought to be a simple vasomotor reaction [1] which would involve nerve fibers passing upward from the medulla to the arteries in question. Such an interpretation was supported by the work of Cobb and Finesinger [2] and of Chorobski and Penfield.[3]

Despite these observations, the exact conditions determining the arterial dilation were not fully understood. In some experiments the caliber of the arteries seemed to be affected by changes in the blood pressure, the respiration or the strength of the stimulus; in others, no such relationship could be made out. Furthermore, it was difficult to reconcile our observations with those of other workers, notably Schmidt.[4]

During the past two years we have studied the problem again with the hope of obtaining a clearer understanding of the conditions underlying this vascular response. Several of the conditions can now be described more accurately. Recent observations have led to a wholly new conception of the mechanism of cerebral vasodilation. The pial arteries dilate not only after stimulation of the vagus nerve but also after

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3. Chorobski, J., and Penfield, W.: Cerebral Vasodilator Nerves and Their Pathway from the Medulla Oblongata, Arch. Neurol. & Psychiat. **28**:1257 (Dec.) 1932.

4. Schmidt, C. F.: The Intrinsic Regulation of the Circulation in the Parietal Cortex of the Cat, Am. J. Physiol. **114**:572 (Feb.) 1936.

stimulation of the depressor (aortic) and carotid sinus nerves, and if they are thus dilated, they constrict again (presumably to their normal caliber) when the blood pressure is raised. The reaction is not peculiar to nerve stimulation; it occurs under a wide variety of conditions that are apparently unrelated but have one feature in common, namely, the behavior of the arterial pressure. Whenever the blood pressure falls below a critical level (and the blood flow through the brain is correspondingly retarded), the arteries on the surface of the brain dilate. This happens with great regularity regardless of the cause of the fall in blood pressure, though the critical level appears to vary with the individual animal and, to some extent, with the physiologic state of the animal.

METHOD

Our present method of investigation was similar to that used in the earlier study—measurement of changes in the diameter of the pial arteries through a cranial window.[1] In addition, a photokymograph[5] was used to obtain more accurate records of variations in the cerebrospinal fluid pressure, the blood pressure, the respiration and the arterial diameter. All these were recorded directly from the manometers, except the diameter of the artery. This was measured by an observer at the microscope who gave the measurements verbally to an assistant. The latter was seated at the kymograph before a vertical scale 10 cm. in length having figures similar to those on the ocular scale of the microscope. As each number was given by the observer, the assistant at once moved a marker, by means of a rack and pinion attachment, up or down the vertical scale. The position or path of the marker was recorded on the sensitized paper of the kymograph. The delay between observation and record by this method was seldom more than two or three seconds. The observer could give his undivided attention to the microscope and give readings as rapidly as measurable changes were seen.

For anesthesia 0.5 cc. of dial[6] per kilogram of body weight (by intraperitoneal injection) was used chiefly, though in a few instances pentobarbital sodium or amytal was used. In this investigation 159 cats, 3 monkeys and 2 dogs were studied.

For stimulation either a unipolar silver electrode (the second electrode being grounded in muscle) or bipolar silver electrodes were used with a Harvard inductorium and one dry cell. The stimulation was usually applied for one minute, sometimes for only thirty seconds, and the coil distance varied from 7 to 13 cm. (usually 9 to 12 cm.).

Comment on Method.—Several variables were recognized as the work progressed, and as far as possible these were either controlled or recorded.

The state of the arterial wall prior to any experimental procedure proved to be an important factor which largely determined subsequent

5. The kymograph, which uses 50 feet (1,500 cm.) of bromide paper, is a modification of the apparatus described by Deissler, Higgins and Sheard (Simple Photographic Recording Kymograph, Science **81**:619 [June 21] 1935).

6. The dial was supplied by Ciba Company, Inc., New York.

changes in caliber. When the wall was relaxed and the vessel already dilated, a fall in blood pressure often caused narrowing of the lumen. Failure to appreciate this fact led to errors in the interpretation of our earlier results. It seems probable that some of the conflicting results of Ask-Upmark [7] and other workers in this field can be explained on this basis. The arteries often became dilated, owing to asphyxia of mild degree, to trauma (due either to the operative procedure or to contact between the surface of the brain and the glass of the window) and to low blood pressure from any cause. The effect of trauma to the vessel walls was lessened by improvements in technic.

The effective strength of the stimulation also influenced the results. Obviously this depended not only on the strength of the current passing between the electrodes but also on the state of the nerve stimulated, on the depth of anesthesia and probably on other unknown factors in the physiologic condition of the animal.

Still another variable, and a potential source of error, was the occasional spread of current to the cervical sympathetic nerve, due either to insufficient dissection of the vagus nerve or to the presence of communicating branches between the vagus and sympathetic ganglia. In our recent experiments care was taken to note whether the pupil dilated. The results of trials in which this occurred were discarded.

The effects of respiratory change were recorded by the photokymograph or were controlled by artificial respiration and a widely opened thorax. Short periods of apnea or of hyperpnea occurred sometimes during stimulation of the vagus nerve, and these, by altering slightly the carbon dioxide tension of the arterial blood, probably affected the tone of the vessel walls and thus influenced changes in caliber to a variable extent; yet we have been unable to find any striking or consistent differences in the dilator response, whether the animal was or was not under artificial respiration (fig. 1).

The changes in the cerebrospinal fluid pressure chiefly reflected changes in the intracranial venous pressure, and these, in turn, reflected changes in the systemic venous pressure.[8] With natural respiration and thorax intact, the respiratory changes strongly affected the cerebrospinal fluid pressure, and even with artificial respiration and an open thorax similar changes of less degree were often seen. There was no constant relationship between changes in the arterial caliber and changes in the cerebrospinal fluid pressure.

Before further discussion of changes in the caliber of the vessels, it may be well to define two adjectives used in describing such changes.

7. Ask-Upmark, E.: The Carotid Sinus and the Cerebral Circulation, Acta psychiat. et neurol., supp. 6, 1935.

8. Fremont-Smith, F., and Kubie, L. S.: A. Research Nerv. & Ment. Dis., Proc. **8**:104, 1929.

namely, "active" and "passive." When speaking of "active" dilation we mean an increase in caliber with no rise in arterial pressure. Presumably this type of dilation is due to relaxation of the muscular coats of the artery, allowing a minimum of intravascular pressure to push the walls outward. The pressure necessary to do this appears to be surprisingly low. In arteries in the pia we have seen a state of nearly maximal dilation maintained when the pressure in the femoral artery fell to 15 mm. of mercury. By the term "passive" we mean distention of the arterial walls by a rising arterial pressure. When the tone of the arterial muscle is normal little if any such passive dilation occurs unless the rise in pressure is excessive and abrupt.

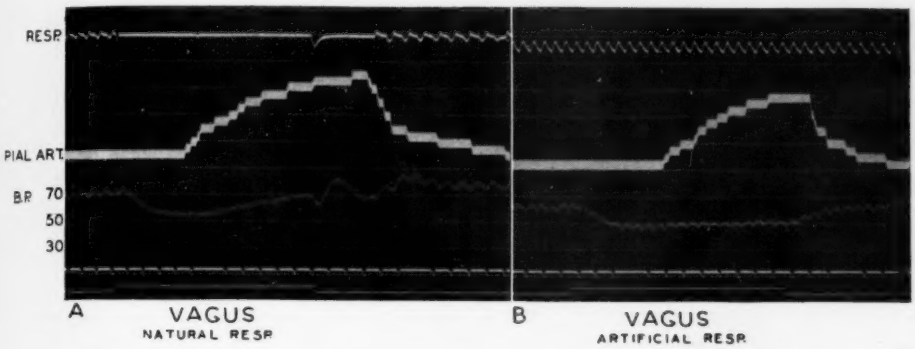

Fig. 1.—Stimulation of the vagus nerve. Conditions: bilateral section of the vagus, depressor and cervical sympathetic nerves; and faradic stimulation of the left vagus nerve (cephalic end) with embedded bipolar electrodes (coil distance, 11 cm.). *A*, natural respiration: The blood pressure (femoral artery) fell to 56 mm., and the pial artery (during a long period of apnea) dilated from 210 to 300 microns. *B*, artificial respiration and a widely opened thorax: The blood pressure fell to 48 mm., and the artery dilated as in *A*, though the respiration was now controlled. In this figure and in the succeeding ones the signal line is at the bottom. Next is the time marker, recording five second intervals.

OBSERVATIONS

In a large series of experiments on 164 animals, pial arteries from 100 to 300 microns in diameter were measured. Dilation was the chief response of these vessels (under conditions which will be described later) to faradic stimulation of any of the following structures: (1) the cephalic end of the cut vagus nerve (figs. 1 and 2), (2) the cephalic end of the depressor (aortic) nerve, (3) the carotid sinus nerve, (4) the surface of the carotid sinus (fig. 3) or (5) the surface of the common carotid artery, within 1 cm. of the sinus (but not lower in the neck).

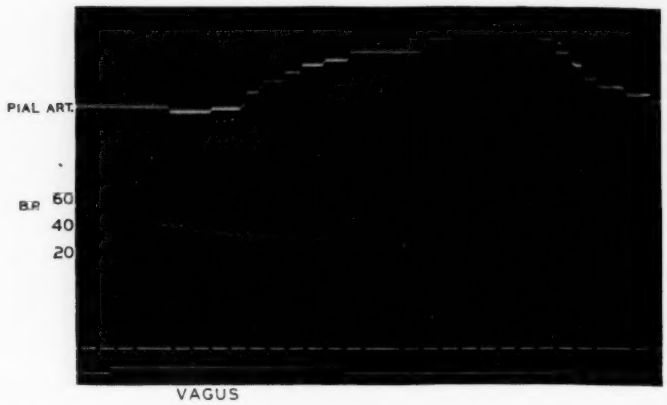

Fig. 2.—Stimulation of the vagus nerve. Conditions: bilateral section of the vagus, depressor and cervical sympathetic nerves; artificial respiration (widely opened thorax), and faradic stimulation of the left vagus nerve (cephalic end) with embedded bipolar electrodes (coil distance, 8 cm.). The blood pressure (femoral artery) fell to 30 mm., and the pial artery, after slight constriction, dilated from 225 to 322 microns.

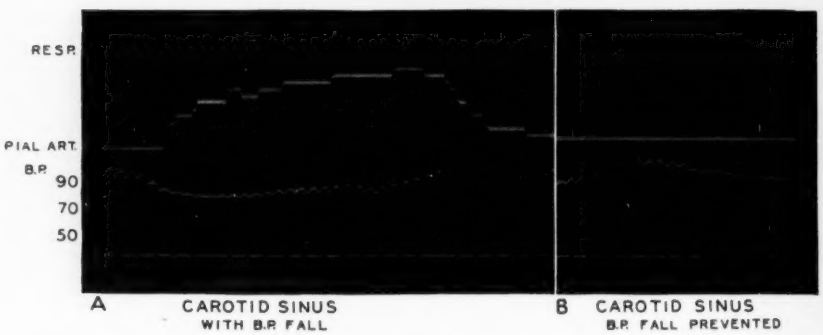

Fig. 3.—Stimulation of the carotid sinus nerve. Conditions: exposure of the left carotid sinus without injury to the sinus nerve; denervation of the right carotid sinus; bilateral section of the vagus, depressor and cervical sympathetic nerves; artificial respiration (widely opened thorax), and faradic stimulation of the left carotid sinus body with a unipolar electrode, the other electrode being placed in a muscle of the leg (coil distance, 11 cm.). *A*, the blood pressure (femoral artery) fell to 82 mm., and the pial artery dilated from 127 to 217 microns. *B*, the blood pressure was prevented from falling by the injection of warm Ringer's solution into the superior mesenteric artery. Actually the pressure was raised 16 mm. during the stimulation by accidental overcompensation. The pial artery did not dilate.

Occasionally, when the blood pressure was low, we noticed rhythmic or irregular dilations of the pial arteries, recurring sometimes every ten seconds, sometimes every one or two minutes (fig. 4).

It is interesting that even when the records of the blood pressure and respiration showed no fluctuations during these "spontaneous" changes in arterial caliber, there was visible a definite decrease in the velocity of blood flow in these vessels preceding each dilation. Just before the arteries constricted, at the end of the dilation, the flow increased once more. This happened again and again, with no visible change in the pressure (as recorded from the femoral artery), showing that the latter was not an invariable index of the rate of blood flow through the cerebral arteries.

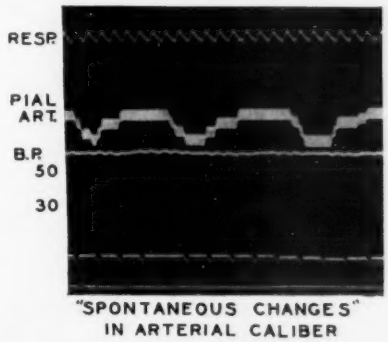

Fig. 4.—Spontaneous changes in the caliber of the pial artery. Conditions: section of the left vagus, depressor and cervical sympathetic nerves, and artificial respiration. The rhythmic changes in diameter (from 135 to 157 microns) began to appear in this pial artery when the slowly falling blood pressure had reached 60 mm. No electrical stimulation or other experimental procedure initiated these changes, and the respiration was regular; also, the record shows no fluctuations of pressure in the femoral artery. However, under similar conditions we have observed a sudden slowing of flow in the pial arteries just before each dilation.

In addition to electric excitation of the structures already enumerated, we found that a similar vasodilator reaction in the pia was closely associated with low blood pressure under such diverse conditions as (*a*) hemorrhage (fig. 5), (*b*) obstruction of the cardiac action (by increasing the pericardial pressure), (*c*) downward traction on either carotid artery (without occlusion) and (*d*) destruction of the spinal cord (midcervical region).

Several questions arose concerning this arterial response in the pia. Was it a composite or a simple reaction? Was the response to stimulation of the vagus nerve similar to that after stimulation of the carotid sinus and other nerves? What mechanism or mechanisms were involved?

Depending on a variety of conditions, the usual reaction to an effective stimulation of the vagus nerve was as follows: Within from fifteen to thirty-five seconds of the beginning of the stimulation, the pial arteries started to dilate. After a gradual (or abrupt) increase in diameter they regained their normal size in from one to three minutes (figs. 1 and 2). The dilation was sometimes interrupted by partial

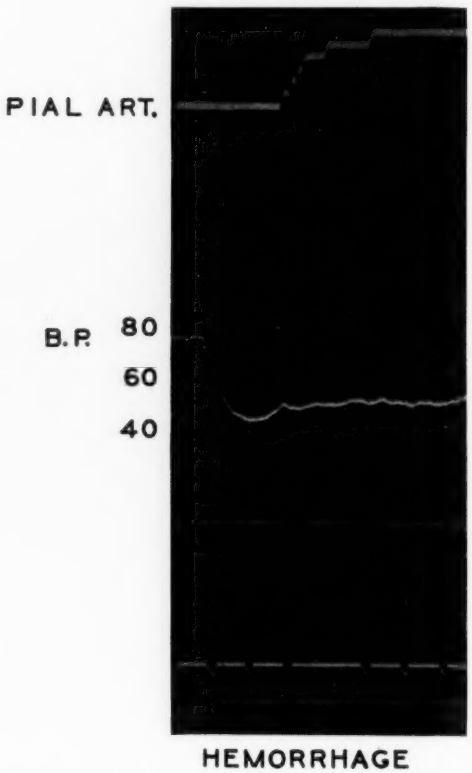

Fig. 5.—The effect of hemorrhage on the caliber of the pial artery. Conditions: bilateral section of the vagus, depressor and cervical sympathetic nerves, artificial respiration and an open thorax. Twenty cubic centimeters of blood was removed by syringe from the celiac axis artery. The blood pressure fell to 42 mm., and the pial artery dilated from 180 to 225 microns.

constriction followed by a second increase in caliber, or the dilation was delayed until after the stimulation was over and the blood pressure was rising. The latter dilation was chiefly a "passive" change, aided sometimes by a period of apnea. Frequently, before the onset of the main dilation there was a brief preliminary constriction, lasting from five to fifteen seconds, during the rapid fall in blood pressure. This constriction was mainly "passive" (partial collapse). When the initial

pressure was high, however, dilation due to the stimulation seldom occurred (fig. 6). Nevertheless, in the vast majority of cases when the blood pressure fell to 50 mm. of mercury, frank dilation resulted.

The precise blood pressure level at which the dilation occurred varied considerably in different animals, but it proved to be fairly constant for each individual animal.[9] This so-called "critical level" (that is, the point at which the main dilation of the artery began) ranged in the majority of the experiments between 50 and 80 mm. of mercury (fig. 7). Occasional minor dilations were seen even though the blood pressure did not fall to the "critical level."

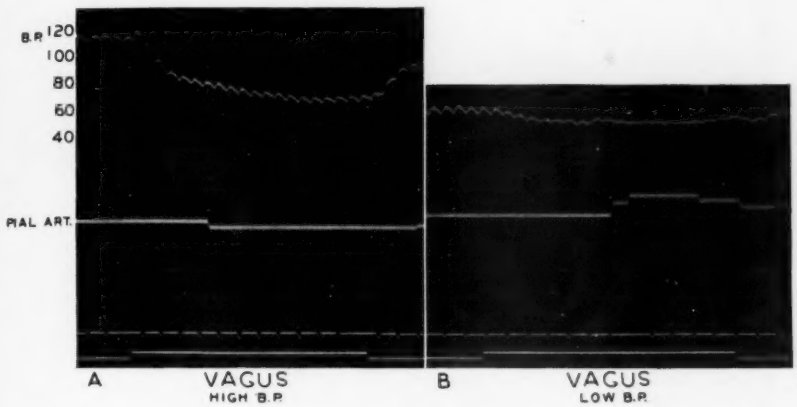

Fig. 6.—Stimulation of the vagus nerve, showing the contrasting effect of a high and a low blood pressure. Conditions: section of the left vagus, depressor and cervical sympathetic nerves; artificial respiration (open thorax, diaphragm cut), and faradic stimulation of the left vagus nerve (cephalic end) with embedded bipolar electrodes (the coil distance in *A* was 10 cm.; in *B*, 13 and then 11 cm.). *A*, the blood pressure (femoral artery) fell 46 mm. during the stimulation, but the lowest point reached was only 68 mm. The pial artery did not dilate. *B*, the blood pressure fell only 10 mm. during the stimulation, but the low point was then 50 mm. The artery dilated from 195 to 217 microns. Between *A* and *B* 15 cc. of blood was removed from the superior mesenteric artery to lower the blood pressure. The lower level of pressure rather than the extent of the fall proved to be the deciding factor in the dilation of the pial artery.

The actual level to which the blood pressure fell and the length of time during which it stayed down seemed to be the most important factors in causing a maximal dilation of the artery. If the low pressure

9. An exception to this last statement should be mentioned. If an animal was subjected to repeated hemorrhages (at intervals of fifteen minutes or so), the "critical level" rose progressively. This may have been due to dilution of the blood and loss of hemoglobin. To maintain a given oxygen tension in the tissues under these conditions would require a faster blood flow (and higher blood pressure) than when the percentage of hemoglobin was normal.

persisted for thirty seconds or longer, the dilation was sometimes striking. When the pressure began to rise, the artery dilated passively still further (fig. 2). While the pressure was still rising (or after it had regained its previous level), the artery constricted again to its original caliber. The blood flow during the first phase of the dilation (before the pressure started to rise) was still visibly slow, and it was not until the pressure rose that the rate of flow noticeably increased.

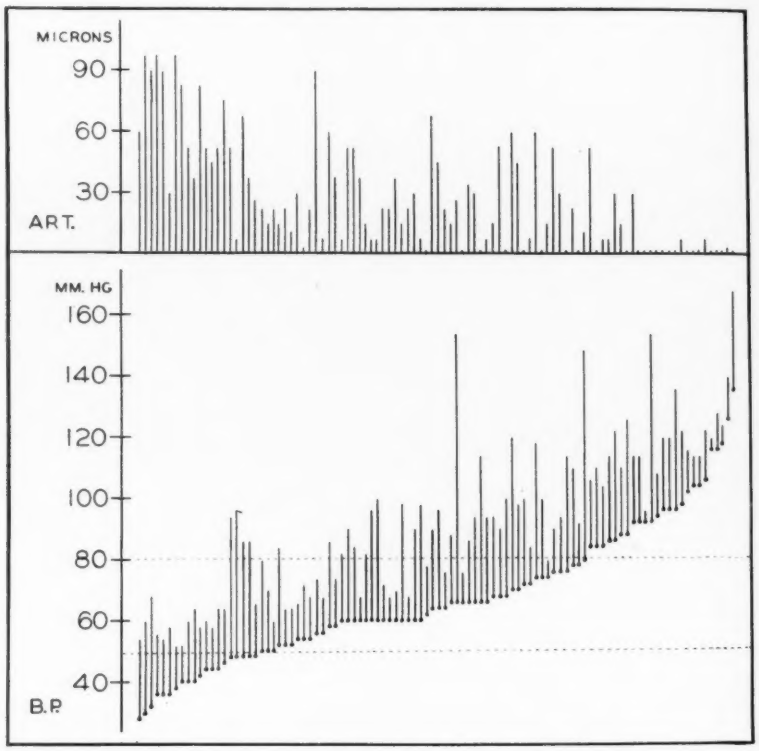

Fig. 7.—Stimulation of the vagus nerve, showing the relation between the level of the blood pressure and the amount of arterial dilation in the pia. Each line in the lower group shows the actual amount of fall in blood pressure during a single stimulation. The lowest level reached in each experiment is stressed by a dot at the end of the line, and the experiments are arranged in ascending order according to these low points. Each upper line represents the amount of increase in diameter of a pial artery, corresponding to the level of blood pressure in the same experiment directly beneath. Ninety-nine experiments from the last 27 cats of our series are shown in this chart. In all of these we have records by the photokymograph. It can be seen at a glance that when the blood pressure falls below 50 mm., the dilations are greatest. On the other hand, when it falls only to 80, the dilations are negligible. Between these two points the degree of dilation varies widely, owing to the fact that the "critical level" (at which dilation appears) differs in different animals. The dotted lines indicate the zone within which most of the "critical levels" fall.

In order to secure more evidence as to the effect of blood pressure on vasodilation, we decided, first, to prevent any fall in pressure during stimulation of the vagus nerve and, second, to cause a simple fall in pressure without stimulation of any kind.

Compensation to prevent a fall in blood pressure was attempted in various ways. Clamping the thoracic aorta several minutes before the stimulation was not entirely successful, because in spite of it the arterial pressure in the head sometimes fell. Nevertheless, in about 75 per cent of the experiments in which the aorta was clamped and the vagus nerve then stimulated, no dilation of the pial artery occurred. Partial constriction of the thoracic or of the abdominal aorta, just as the stimula-

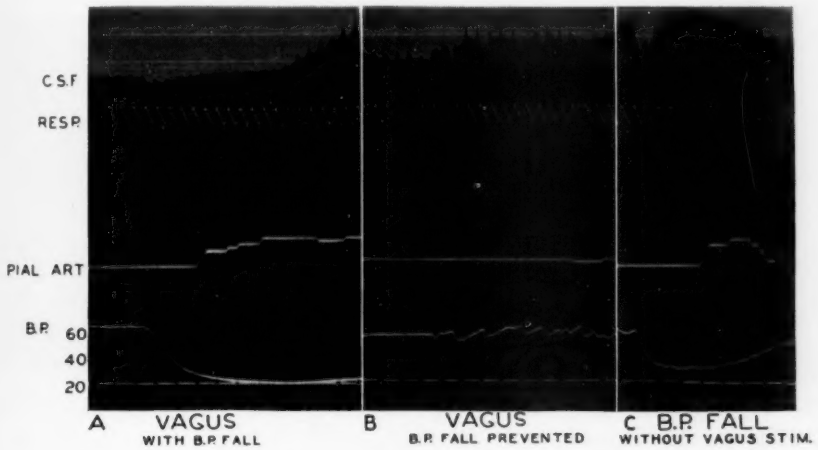

Fig. 8.—Stimulation of the vagus nerve, with and without a fall in blood pressure, compared with a simple fall in blood pressure without nerve stimulation. Conditions: section of the left vagus, depressor and cervical sympathetic nerves; ligation of the right carotid artery (the blood pressure was recorded from the cephalic end of this artery); artificial respiration (open thorax), and faradic stimulation of the left vagus nerve (cephalic end) with embedded bipolar electrodes (coil distance, 8 cm. in *A* and *B;* no stimulation in *C*). *A,* the blood pressure fell to 22 mm., and the pial artery dilated from 127 to 165 microns. *B,* during this stimulation of the vagus nerve the blood pressure in the head was prevented from falling by partial occlusion of the thoracic aorta. The pial artery did not dilate. *C,* the aorta was unclamped, causing a transient fall in the blood pressure (head) to 32 mm. There was no stimulation of the vagus nerve. The pial artery dilated to the same extent as in *A*. In this figure and in figure 9 the cerebrospinal fluid pressure taken from the cisterna magna is recorded in millimeters of water by fluctuation of the meniscus in a 1 mm. bore manometer.

tion started, proved a more successful method of compensation. The injection of heparinized blood or of Ringer's solution into the aorta through the superior mesenteric artery proved to be the best method of keeping up the pressure with the least fluctuation. Under these condi-

tions the fall in blood pressure was entirely prevented, and in every case in which this succeeded the pial artery failed to show the usual dilation (figs. 3 and 8).

Still another method of preventing a fall in the blood pressure during stimulation was attempted by cutting the spinal cord in the midcervical region. This procedure alone often caused such a fall in pressure that the artery dilated and remained in this condition. Occasionally the pressure did not fall so far, or we were able to raise it again by partial occlusion of the abdominal aorta. In these instances, during stimulation of the vagus nerve the blood pressure did not fall and the pial artery did not dilate (fig. 9).

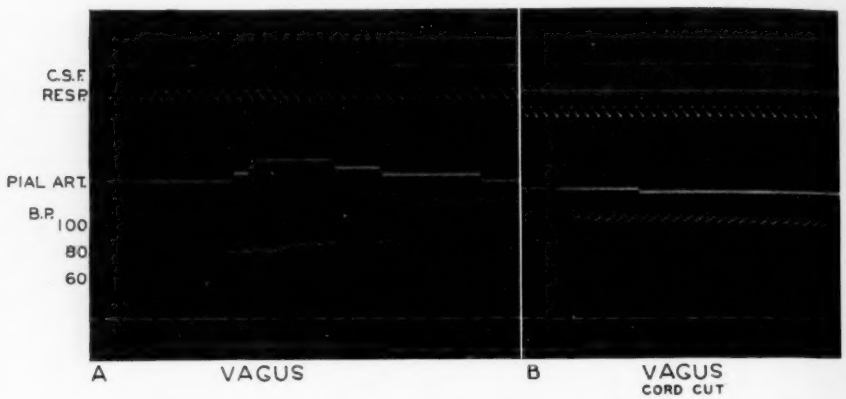

Fig. 9.—Stimulation of the vagus nerve before and after the spinal cord was cut. Conditions: section of the left vagus, depressor and cervical sympathetic nerves; artificial respiration (open thorax), and faradic stimulation of left vagus nerve (cephalic end) with embedded bipolar electrodes (coil distance, 11 cm. in *A* and *B*). *A*, the blood pressure (femoral artery) fell to 80 mm., and the pial artery dilated from 255 to 277 microns. In spite of the open thorax, the cerebrospinal fluid pressure rose as the blood pressure fell and remained elevated during the stimulation. *B*, the spinal cord was cut between the third and fourth cervical vertebrae one hour before record *B* was taken. The blood pressure, which fell after the cord was cut, was raised to its former level by partial occlusion of the abdominal aorta. The pressure was then measured in the celiac axis artery. Stimulation of the vagus nerve then caused no change in the blood pressure or in the cerebrospinal fluid pressure. The pial artery did not dilate.

Thus, it seemed to be clear that the characteristic vasodilation bore a definite relation to the blood pressure, or more specifically to the pressure in the cerebral arteries and to the rate of blood flow through them.

In order to rule out the chance that some dilator substance might have been formed in the viscera during the period of sluggish flow through it, we partly clamped the thoracic aorta, greatly retarding the flow through all vessels below the diaphragm and accelerating the flow

through the head. No dilation of the pial arteries occurred unless the clamp was tightened suddenly; then, with the sharp rise of blood pressure in the head, the pial arteries showed temporary and "passive" dilation. Within one or two minutes, however, while the blood pressure in the head remained extremely high and the flow through the viscera was still retarded, the arteries constricted, usually below their initial caliber.

To test this point further and see whether a lowering of pressure in the head alone (together with retardation of the flow) was the important factor, we placed a screw clamp on the carotid and subclavian arteries, just above the aortic arch. By gradually closing this clamp we could lower the arterial pressure in the head at will. When the

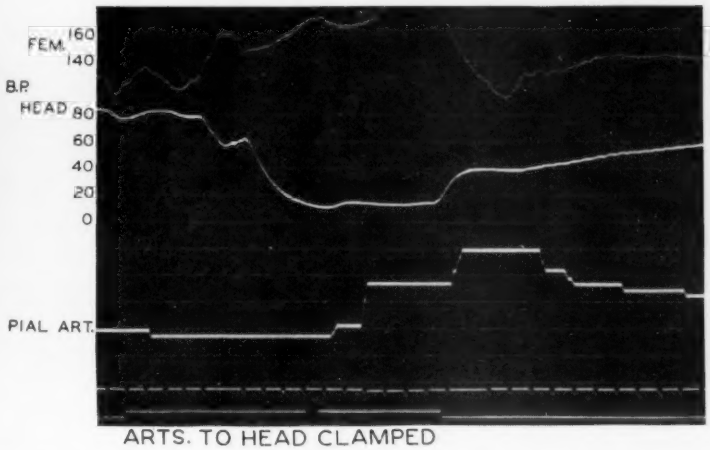

Fig. 10.—The effect of lowering the blood pressure in the head. Conditions: bilateral section of the vagus, depressor and cervical sympathetic nerves; the placing of a screw clamp on both carotid and subclavian arteries, in readiness to occlude the latter; recording of the blood pressure from the femoral artery (upper tracing) and from the cephalic end of the right carotid artery (second tracing), and artificial respiration (open thorax). Occlusion of the carotid and subclavian arteries caused a fall of blood pressure in the head to 12 mm. The flow through the pial artery became very much slower, and there was dilation from 172 to 225 microns. The clamp was then released; the blood pressure in the head rose, and the artery dilated still further to 262 microns. Within twenty seconds of the time when the rate of flow had noticeably increased, the artery began to constrict rapidly while the blood pressure in the head slowly continued to rise. The inverse relationship between the pressure in the arteries of the head and the pressure in the femoral artery is explained by the situation of the clamp. The break in the signal line designates the point at which definite slowing of the flow in the pial arteries was first observed.

pressure in the carotid (cephalic end) fell to 30 mm. of mercury and the flow through the pial arteries was visibly slowed, these vessels showed the characteristic dilation (fig. 10).

COMMENT

In an earlier series of experiments, by Wolff and Forbes,[10] it was shown that when the region of retarded blood flow was limited to the brain and meninges (by raising the intracranial pressure nearly to the level of the diastolic blood pressure), the pial arteries dilated. It seems probable that this reaction can be fully explained as an effect of tissue asphyxia (stagnant anoxia). Though the blood pressure was actually elevated in these experiments, the slowing of the flow produced the same effect on the arteries that we have observed in our recent experiments.

Early in the investigation the question arose as to what other nerve pathways, besides the vagus nerve, might be involved in the observed dilation of pial arteries. We found that stimulation of the vagus nerve caused the usual dilation (with a fall in pressure)[11] even under the following conditions: (1) after bilateral section of the vagus, depressor, cervical sympathetic and carotid sinus nerves; (2) after section of the ipsilateral seventh nerve and removal of the superior cervical ganglion on the same side, or (3) after local irrigation with cocaine (either a 1 or a 2 per cent solution) or procaine hydrochloride (1 per cent) over the surface of the arachnoid beneath the cranial window.

If nerve terminals on the arteries in this region had been responsible for their dilation under the condition described, local anesthesia should have abolished the reaction.

In these experiments we were convinced by repeated observations that dilation of arteries in the pia did not cause a faster flow through these vessels when there was a coincident fall in blood pressure. In spite of the dilation, the flow was retarded. If this point is borne in mind, the apparent contradiction between Schmidt's and our results is at once explained. Schmidt [4] was recording changes in the rate of flow; we were recording changes in diameter. He found a reduction in the rate of flow through the parietal cortex during stimulation of the vagus nerve and interpreted this to mean arterial constriction. We have observed a similar reduction in flow but, coincident with this, arterial dilation.

Cobb and Finesinger [2] stimulated the vagus nerve after cutting the seventh nerve close to the medulla and obtained no dilation of the pial arteries, though this reaction had occurred before such nerve section. Therefore, it seemed probable that a tract of dilator fibers connected the vagus nucleus with the seventh nerve and then passed upward to the pial arteries.

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10. Wolff, H. G., and Forbes, H. S.: Cerebral Circulation: V. Observations of the Pial Circulation During Changes in Intracranial Pressure, Arch. Neurol. & Psychiat. **20**:1035 (Nov.) 1928.

11. The well known splanchnic vasodilator reflex from the tenth nuclei in the medulla down the cord and out the autonomic nerves to the viscera probably was the cause of the fall in the systemic blood pressure.

We have been unable to confirm this observation. In 14 animals we stimulated the vagus nerve after cutting the seventh nerve proximal to the geniculate ganglion, and in every instance when the blood pressure fell to the "critical" level the pial artery dilated (fig. 12). We have found no difference in the reaction whether the seventh nerve was intact or cut (figs. 7 and 13).

On the whole, we believe that the main reaction which we are studying is caused by a relatively simple process rather than by a number of diverse processes. We mean by this that although the fall in blood pressure may be initiated in many different ways, the subsequent mechanism is probably the same in all cases; a slow blood flow through the brain, with relaxation of the walls of the arteries, causing these arteries to dilate.

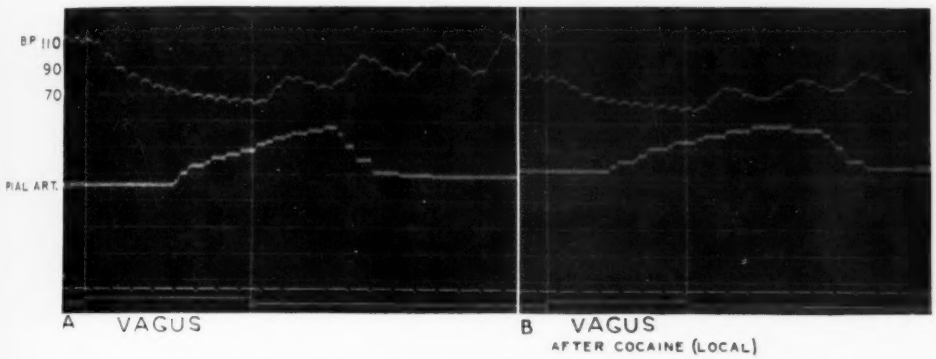

Fig. 11.—Stimulation of the vagus nerve before and after the local administration of cocaine hydrochloride. Conditions: section of the left vagus, depressor and cervical sympathetic nerves; artificial respiration (open thorax), and faradic stimulation of the left vagus nerve (cephalic end) with embedded bipolar electrodes (coil distance, 10 cm.). *A*, the blood pressure (femoral artery) fell to 65 mm., and the pial artery dilated from 165 to 232 microns. *B*, cocaine hydrochloride was applied locally beneath the cranial window three and one-half minutes before record *B* was taken. A 0.5 cc. of a 1 per cent solution was used. The blood pressure fell to 60 mm., and the pial artery dilated as before. The vagus nerve was stimulated again twenty-seven minutes after the cocaine was administered, and the reaction was similar to that shown here.

Although the main reaction may thus be accounted for, our observations suggest that the situation is complicated by one or more additional factors. It has already been mentioned that minor dilations sometimes occur when the blood pressure falls only to 90 mm. of mercury.

It seems probable that a moderate fall in the blood pressure may slightly relax the arterial walls, not enough to cause "active" dilation

but enough to assist in bringing about a "passive" dilation when the blood pressure rises, even slightly.

Finally, there remains the question: How does a decrease in the velocity of the blood flow through these arteries cause relaxation of their walls and consequent dilation? The capillaries and venules might be expected to dilate when the flow is retarded, since the blood in these vessels becomes much more "venous," but why should the arteries dilate? The arterial blood has neither an abnormally low oxygen content nor a high carbon dioxide content.[12] Five explanations may be offered:

1. Nerve endings on the venules may be stimulated by an excess of carbon dioxide or by a low oxygen tension and through a local (axon) reflex between venules and arteries cause the arteries to dilate.

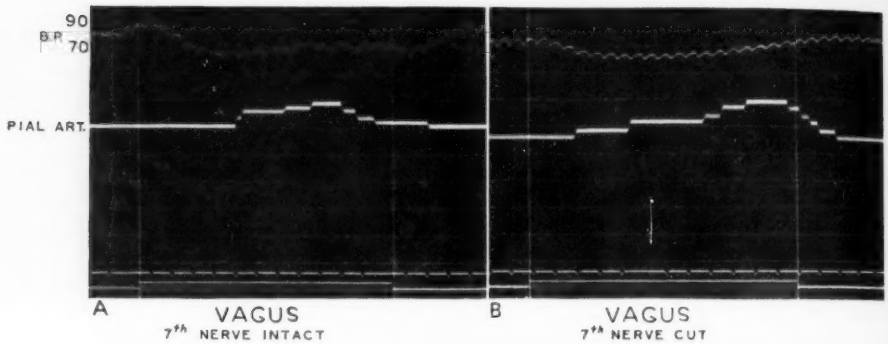

Fig. 12.—Stimulation of the vagus nerve before and after the seventh nerve was cut proximal to the geniculate ganglion. Conditions: section of the left vagus, depressor and cervical sympathetic nerves; artificial respiration (open thorax), and faradic stimulation of the left vagus nerve (cephalic end) with embedded bipolar electrodes (coil distance in *A*, 8 and then 12 cm.; in *B*, 11 cm.). *A*, the blood pressure (femoral artery) fell to 65 mm., and the pial artery dilated from 180 to 210 microns. *B*, the left seventh nerve was cut proximal to the geniculate ganglion half an hour before this record was taken. The blood pressure fell to 62 mm., and the pial artery dilated as before.

This explanation seems improbable, since cocaine applied locally to the arachnoid over the arteries in question does not prevent the usual dilation of these vessels in response to a fall of blood pressure. An axon reflex would be abolished by cocaine.[13]

12. On two occasions determinations were made of the arterial oxygen and the carbon dioxide content. The oxygen was practically unchanged, and the carbon dioxide content was lowered after stimulation of the vagus nerve.

13. Krogh, A.: Anatomy and Physiology of Capillaries, New Haven, Conn., Yale University Press, 1929, p. 124.

2. An increase in the carbon dioxide tension in the tissue cells adjacent to the arteries may diffuse across the intervening space and cause dilation through direct contact. This seems unlikely, owing to the short interval between the onset of the slow blood flow and the dilation. Also, the abruptness and the short duration of the dilation seem incompatible with diffusion.

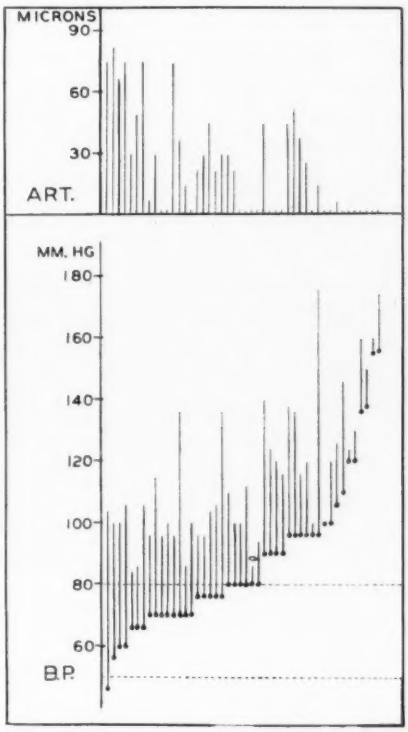

Fig. 13.—Stimulation of the vagus nerve. The ipsilateral seventh nerve was cut proximal to the geniculate ganglion. The arrangement of this chart is the same as that of figure 7 and includes the fourteen experiments in which the left vagus nerve was stimulated after the left seventh nerve was cut proximal to the geniculate ganglion. Comparison with figure 7 will show no essential difference in the response after section of the facial nerve near the medulla.

3. Metabolites (lactic acid, for example) accumulating in the brain under conditions of low oxygen tension may be absorbed by the cerebral capillaries, carried through the heart and lungs and returned to the pial arteries, relaxing their walls. This explanation, too, seems improbable for several reasons.

4. Elimination of the carbon dioxide produced locally by the muscle fibers of the arterial wall (as well as entrance of oxygen to the

muscle) probably takes place by diffusion from the lumen of the vessel, since arteries in the pia smaller than 800 microns have no vasa vasorum. It is conceivable, therefore, that a decrease in the velocity of the flow through the lumen would retard the gaseous exchange sufficiently to relax the muscle fibers and bring about dilation through the products of their metabolism.

5. A simpler explanation may be that of Bayliss.[14] He suggested that relaxation of arterioles in response to a fall of blood pressure (as well as contraction in response to increased tension) might be explained as a characteristic of smooth muscle, for it is known to react in a similar manner in other organs.

SUMMARY

Stimulation of the vagus, carotid sinus and depressor nerves is followed under certain conditions by dilation of the arteries in the pia.

The one condition which seems to be essential is a fall in the blood pressure to a low level. When the pressure falls to a level that is critical for the individual animal (usually about 60 mm. of mercury), the arteries dilate. Conversely, when the pressure rises the dilated arteries constrict and soon regain their normal caliber.

If the fall of pressure is prevented (by some method of compensation), the arteries do not dilate.

A simple fall of blood pressure produced by any means, such as hemorrhage, causes dilation similar to that which follows stimulation of "depressor" nerves.

It seems, therefore, that the relation of the vagus, carotid sinus and depressor nerves to vasodilation in the pia is indirect, their stimulation causing (through the medulla, cord and autonomic nerves) a reflex splanchnic vasodilation, with a consequent fall in blood pressure, and it is only by this fall that the cerebral vessels are affected.

The immediate cause of arterial dilation in the pia appears to be a sudden slowing of the blood flow (due to the lowered pressure) through these vessels.

This vascular reaction must act as an important safety device, allowing the cerebral cortex to obtain more oxygen than would otherwise be possible when the blood pressure falls to a dangerously low level.

NOTE.—After this article had gone to press further experiments showed that stimulation of the facial nerve was accompanied with dilatation of the pial arteries without a fall in blood pressure. This reaction appears to be distinct from that following stimulation of "depressor" nerves. It will be described in a subsequent paper.

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14. Bayliss, W. M.: The Vasomotor System, London, Longmans, Green & Co., 1923, p. 14.

CEREBRAL CIRCULATION

THE REACTION OF THE PIAL ARTERIES TO A FALL IN BLOOD PRESSURE

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Since the introduction of the use of the cranial window by Forbes,[1] study of the vasomotor reaction of the pial arteries has been productive of a number of important results. Not only the influence of chemical substances on these arteries has been revealed but also the effect of changes in the composition and osmotic concentration of the blood and the effect of the stimulation of various nerves. Simultaneously with the influence which these diverse forces exert on the cerebral arteries, however, there are frequently universal vasomotor reactions and consequent changes in both the arterial and the venous blood pressure; therefore, it is necessary to investigate what effect changes in the endovascular pressure itself have on the pial arteries. Both in this and in several subsequent articles, the question as to the relationship between the arterial blood pressure and the tonus of the pial arteries will be discussed.

The reaction of the pial arteries during a fall in blood pressure has been the subject of previous study. Donders[2] noted anemia of the cerebral arteries when the animals on which he was experimenting suffered a loss of blood. By irritating the vagosympathetic nerve fibers in dogs Callenfels[3] produced contraction of the pial arteries in one experiment and in another a contraction which was rapidly replaced by dilation. By means of central irritation of the vagus nerve, Hürthle[4] caused a drop in blood pressure in fifteen cases. Yet the change in the relationship between the pressure in the central portion and that in the peripheral ends of the carotid arteries was not such as to justify assuming the presence of a reaction in the cerebral arteries. On the

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This investigation was aided by a grant from the Rockefeller Foundation.

1. Forbes, H. S.: The Cerebral Circulation: I. Observation and Measurement of Pial Vessels, Arch. Neurol. & Psychiat. **19**:751 (May) 1928.

2. Donders, F. C.: Schmidt's Jahrb. d. in- u. ausländ. ges. Med. **69**:161, 1851.

3. Callenfels, Van der Beke: Ztschr. f. rat. Med. **7**:157, 1855.

4. Hürthle, K.: Arch. f. d. ges. Physiol. **44**:561, 1889.

other hand, by irritating the depressor nerve he found signs of dilation three times, of contraction three times and of unaltered resistance in the cerebral arteries eleven times.

Bayliss and Hill [5] undertook severe stimulation of the peripheral ends of the vagus nerves and observed changes in the cerebral venous pressure. This led them to the conclusion that the pial arteries react "passively"; that is, their lumen decreases during a drop in blood pressure.

While both the primitive observations of the superficial cerebral blood vessels and the indirect conclusions based on the measurement of the pressure in the cranial vessels have given only incomplete information about the vasomotor reactions of the cerebral blood vessels, the cranial window of Forbes permits the exact measurement of the extent of these reactions.

Forbes and Wolff [6] found slight dilation of the pial arteries during irritation of the vagus nerve. Cobb and Finesinger [7] attained the same result on central irritation of the vagus (depressor) nerve. They showed likewise that the reaction failed to appear after severance of the facial nerve, which conducts vasodilator impulses to the pial arteries.

Finally, Ask-Upmark [8] observed that irritation of the carotid sinus nerve causes in some cases vasoconstriction and in others vasodilation in the pia. An evaluation of these results will be discussed later.

The purpose of my experiments was to investigate how the pial arteries react during a drop in blood pressure produced in various ways: (1) peripheral stimulation of the vagus nerve (i. e., reduction of cardiac exertion); (2) irritation of the carotid sinus and depressor nerves (i. e., a reduction of the cardiac output), due to peripheral vascular dilation, and (3) venous and arterial hemorrhages (reduction of the volume of blood).

METHOD

Cats weighing from 2.5 to 4.5 Kg. were experimented on. Various anesthetics were used, the dose being graded in accordance with the size of the animal; allylisopropylbarbituric acid (3 or 4 cg. per kilogram), either alone or combined with ethyl carbamate (urethane) (1.5 to 2 cg. of the former with from 30 to 35 cg. of the latter per kilogram) or else with chloralose (1.8 to 2.4 cg. per kilogram). A combination of barbituric acid preparations and ethyl carbamate or chloralose,

5. Bayliss and Hill: J. Physiol. **61**:334, 1865.

6. Forbes, H. S., and Wolff, H. G.: Cerebral Circulation: III. The Vasomotor Control of Cerebral Vessels, Arch. Neurol. & Psychiat. **19**:1057 (June) 1928.

7. Cobb, S., and Finesinger, J. E.: Cerebral Circulation: XIX. The Vagal Pathway of the Vasodilator Impulses, Arch. Neurol. & Psychiat. **28**:1243 (Dec.) 1932.

8. Ask-Upmark, E.: The Carotid Sinus and the Cerebral Circulation, Acta psychiat. et neurol., supp. 6, 1935.

respectively, was used to secure sufficiently deep narcosis through the combined action of small quantities of drugs supposed to affect the subcortical and cortical portions of the central nervous system.

A cranial window was inserted according to the Forbes[1] technic. In all cases, however, the space between the metal ring and the bone was filled with Harvard cement, such as dentists use in securing dental fillings. In this way complete tightness was insured in all cases. The space between the window and the surface of the brain was filled with Ringer's solution (98.6 F.) through the cannulas of the window, which were then closed by means of faucets.

Since the experiments demanded ease of access to both the anterior side of the animal's neck and the cranial convexity, a specially constructed heated table was used which could be rotated around its longitudinal axis and on which the animal's neck was fastened in an open frame. Thus, without moving the animal it was possible first to expose the nerves at the front of the neck, then to insert the window and finally during the experiment to fix the table in a position which from one side permitted the observation of the surface of the pia and from the other, the stimulation of the nerves. A Leitz ultropak microscope with indirect lighting was used for the examination of the pial arteries (magnification, × 110).

Although it had been planned to examine the reactions of the small arterioles, it was found to be unsatisfactory to use an ordinary ocular micrometer for measuring the enlargement of the blood vessels, for this instrument permits the determination only of changes of more than 4.5 microns. In view of this fact a special screw micrometer was employed which has two thin glass slabs, which, by means of a "sled" drawn by a disk with a graduated scale, may be moved in relation to one another. A fine line was scratched on each glass and on one of them a somewhat heavier cross-wise line as well. The lines were parallel and could be moved nearer together or farther apart by turning the disk. The distance between them was read on the scale of the disk. While an artery was being observed the lines were placed exactly above the outer margins of the vessel wall. Care was taken always to measure the same place on an artery (here the heavier cross-line was a useful guide). Moreover, after every reading the lines were moved some little distance apart before a new adjustment was made. This method permits frequent objective measurements. Standardization of the micrometer by means of an objective micrometer showed the exactness of the measurements (within the limits of from 10 to 50 microns, consideration being taken of the mean error) to ±1.23 microns (three times the mean error). In the following work variations in diameter of ±2 microns were considered significant. Arteries were never measured when at the onset of the experiment they were seen to be dilated or spastically contracted and to have an irregular contour owing possibly to mechanical irritation or manipulation when the window was inserted.

When investigating the exact time relationship between the variations in blood pressure and the arterial reactions, it is of decisive importance to be able to record these two variants absolutely synchronously; so it was found to be unsatisfactory merely to write down the variations in diameter observed in order to compare them later with the changes in the blood pressure. It was found better to record them graphically on the rotating cylinder of a kymograph at once, simultaneously with the blood pressure, the time, the pressure of the cerebrospinal fluid and the pulmonary ventilation. The following method of procedure was used: a disk, around which was placed a metal tape measure graduated like the micrometer scale, was fastened beside the microscope. The disk could be turned in relation to a fixed point; an inelastic thread was attached to the other end of the tape measure. By means of pulleys this thread raised or lowered a metal bar bearing

a writing point which marked the cylinder just below the blood pressure indicator (fig. 1). In this way, as soon as a definite arterial diameter was read on the micrometer scale it was possible to record it indirectly. The time between the taking of the measurement and the recording of the notation was merely the observer's reaction time, i. e., about one second. This was insignificant in comparison with the velocity of the motion of the cylinder (from 1 to 1.5 mm. per second). As will be seen from the graphs, a dilation is shown by an upward movement and a contraction by a downward movement. The "points of observation" are shown by the transition from a horizontal to a vertical line.

The blood pressure, after the insertion of a cannula in the femoral artery, was measured by means of a mercury manometer with a float, the pointer of which marked on the roll. The blood was prevented from coagulating by the injection of a dilute solution of leech head extract through the cannula. Control experiments showed that such dilutions of hirudin had no effect on the pial arteries.

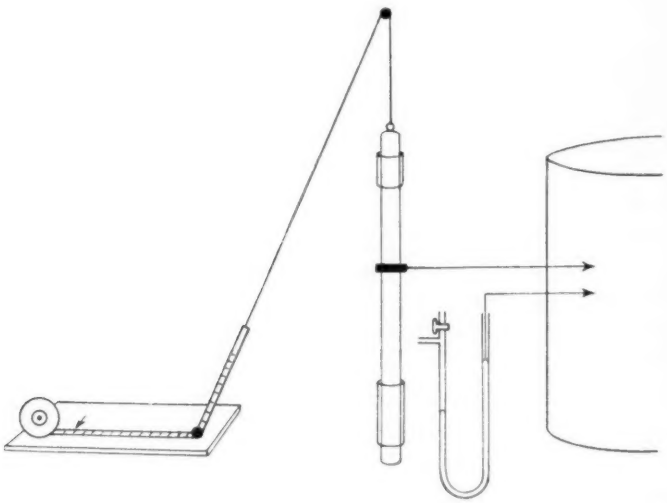

Fig. 1.—Apparatus for registering the diameter of the pial vessels (see text).

The electric stimulations used were either shocks of faradic currents (from 6 to 8 per second) or the pulsating, subdued galvanic current introduced by Hess.[9] According to Hess, it is advantageous to use this current because the autonomic nerves are just as sensitive to it as are the somatic nerves, while the latter are a hundred times more sensitive to a faradic current. Thus, even with fairly strong stimulation produced by a pulsating, subdued galvanic current, it is possible to avoid a muscular reaction and other effects of irradiation.

In several experiments the pulmonary ventilation of the animals was recorded. This was accomplished as follows: Through a tracheal cannula the cat was allowed to breathe spontaneously through water valves. The expired air passed through a gas meter which for every 200 cc. of expired air struck contact and made a record on the cylinder.

9. Hess, W. R.: Beiträge zur Physiologie des Hirnstammes: Die Methodik der lokalisierten Reizung und Ausschaltung subkortikaler Hirnabschnitte, Leipzig, Georg Thieme, 1932.

When the cerebrospinal fluid pressure was measured, it was determined through a cannula in the cisterna magna connected with a water manometer (1.5 mm. amyl). The fluctuations were indirectly recorded in the same way as the diameter of the arteries.

The time was recorded by means of a Richet clock.

In addition, the animals were prepared by exposing the sympathetic, the vagus and the depressor nerves in the neck and isolating the common carotid artery. The sinus nerves were isolated after severance of the hypoglossal nerve, the lingual artery and the digastric muscle.

EXPERIMENTS

A total of eighty-nine falls in blood pressure were produced in twenty animals. In forty-three cases they were brought about by

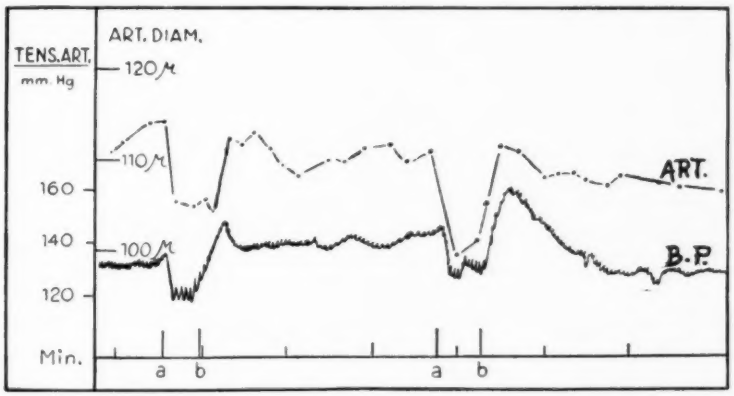

Fig. 2.—Graph showing the reaction of the pial artery during falls in blood pressure of short duration. The interval from *a* to *b* represents the period of stimulation of the peripheral end of the vagus nerve. The diameter of the artery is shown in microns (μ) in the upper tracing; the blood pressure (*Tens. Art.* and *B.P.*) is shown in the lower tracing.

stimulation of the sinus nerves, in two, by stimulation of the depressor nerve and in thirty-four by peripheral stimulation of the vagus nerve. In the remaining ten cases arterial reactions were observed during arterial or venous hemorrhage.

In the first experiments a fall of blood pressure of only short duration was produced. The arteries usually remained passive; i. e., the diameter decreased as the tension grew less and increased as the tension rose (fig. 2). The reactions were independent of whether the fall in blood pressure was caused by peripheral stimulation of the vagus or carotid sinus nerve. Likewise, it was seen that the sinus nerve, ipsolateral to the window, gave the same result as the contralateral nerve.

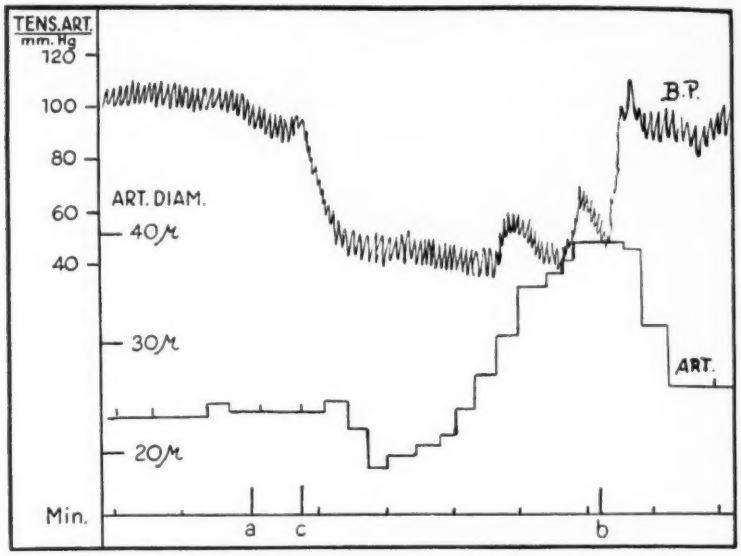

Fig. 3.—The reaction of the pial artery during a fall in the blood pressure of long duration. The interval from *a* to *b* represents the period of stimulation of the carotid sinus nerve. The upper tracing shows the blood pressure (*B. P.*), and the lower one shows the diameter of the artery (*Art.*).

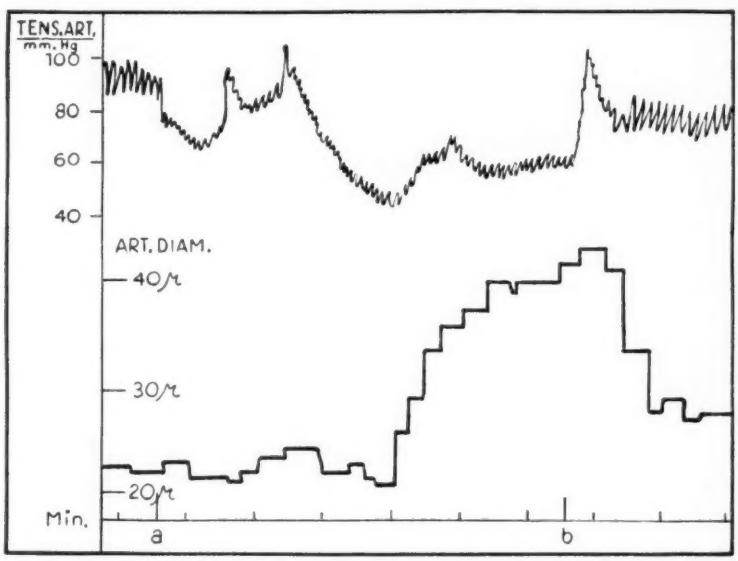

Fig. 4.—The interval from *a* to *b* represents the period of stimulation of the peripheral end of the vagus nerve.

In subsequent experiments, however, falls of blood pressure of more than one minute resulted in an initial decrease in the lumen of the pial arteries which was replaced by considerable dilation, so that the diameter usually became greater than previous to the experiment.

This vasodilatory effect took place also independent of the manner in which the fall in blood pressure was produced. This is illustrated by typical graphs (fig. 3), stimulation of the sinus nerve and (fig. 4) peripheral stimulation of the vagus nerve.

Furthermore, it was seen that during a gradual fall in blood pressure, brought about by repeated withdrawal of 15 cc. of blood from an artery, the arteries dilated progressively as the tension decreased (fig. 5).

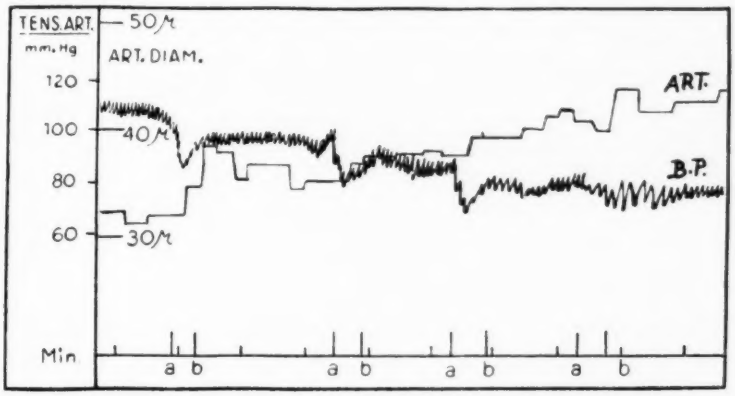

Fig. 5.—The reaction of the artery during repeated removals of blood. Each interval from *a* to *b* represents the withdrawal of 15 cc. of blood.

These observations indicate that the arterial reaction which was observed was a result of the fall in the blood pressure itself and not of a direct reflex released through the vasosensory nerves (carotid sinus and depressor).

In order to investigate this question more closely, all four vasosensory (carotid sinus and depressor) nerves were removed from four animals (in two cases by means of bilateral depressor vagotomy and denervation of the carotis communis and in two by severance of the sinus nerve and depressor vagotomy). In the two latter animals, in order to be sure that the carotid sinus was completely denervated, temporary compression of the carotid artery was attempted; this caused no rise in the systemic blood pressure.

In these four animals stimulation of the peripheral end of the vagus nerve was performed seven times; and the pial arterioles, just as in the aforementioned experiment, showed distinct dilation (fig. 6). Thus,

these results confirm the assumption that it is the fall in the blood pressure itself which causes the reactions in the pial arterioles. In view of this fact, one may regard any fall in blood pressure and the resulting vascular reaction as a joint phenomenon, independent of the way in which the arterial hypotension comes about.

In fifty-three cases a lowering of the blood pressure was caused by a one and a half to a seven minute stimulation of the carotid sinus, depressor or vagus nerves. In a total of thirty-six cases the arteries dilated beyond their usual diameter. In eleven cases the diameter remained unaltered; in six it became smaller. The extent and the

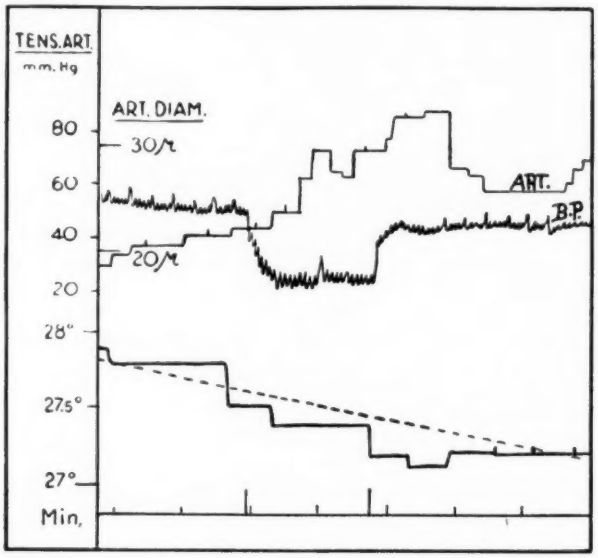

Fig. 6.—The reaction of the artery during a fall in blood pressure and stimulation of the peripheral end of the vagus nerve. The carotid sinus, the (depressor) vagus and the cervical sympathetic nerves had been severed. The "cerebral temperature" is shown in the lower tracing.

direction of the reaction proved to be dependent not only on the height of the blood pressure before the experiment but also on the amount of the fall. The accompanying table gives a summary of the results. They are divided according to the direction and the amount of vascular reaction compared with the fall in blood pressure. The figures for the variations in the blood pressure give the average tension before and the lowest tension during stimulation. In like manner, the average size of the arteries before the experiment is given, as well as the maximum divergence from these figures during the experiment.

Reactions of the Pial Artery to a Fall in Blood Pressure *

Blood Pressure Before Fall, Mm.	Contraction						No Reaction					Dilation					
	Fall in Blood Pressure, Mm. of Mercury			Variations in Diameter, Microns			Fall in Blood Pressure, Mm. of Mercury			Variations in Diameter, Microns		Fall in Blood Pressure, Mm. of Mercury			Variations in Diameter, Microns		
	From	To	%	From	To	%	From	To	%	From	To	From	To	%	From	To	%
About 155	163	3 cases 107	34	59	52	12	151	4 cases 119	21	29	31	147	5 cases 104	29	60	68	13
About 135	140	3 cases 87	38	67	62	7	142	6 cases 91	36	43	43	122	13 cases 82	33	30	34	13
About 90	...	...	..	..	..	..	88	2 cases 62	26	35	37	89	7 cases 59	34	39	48	24
About 75	...	...	..	..	..	..	...	...	..	..	..	75	10 cases 37	50	24	34	40

* The figures in this table are average figures.

The table shows that in cases in which reduction in the endovascular tension lasted for more than one and a half minutes, the arteries contracted in six cases only, and in these the initial blood pressure had been comparatively high. A similar situation was found in those experiments in which, in spite of a 21 to 36 per cent fall in blood pressure, the arteries did not show any change in diameter; ten of twelve cases belonged to the first two groups of the table. In cases in which the initial tension was below 100 mm. of mercury the result of a fall in blood pressure in seventeen of nineteen cases was dilation. This exceeds the reactions in the first two groups (in which the initial blood pressure exceeded 100 mm.) by a high percentage.

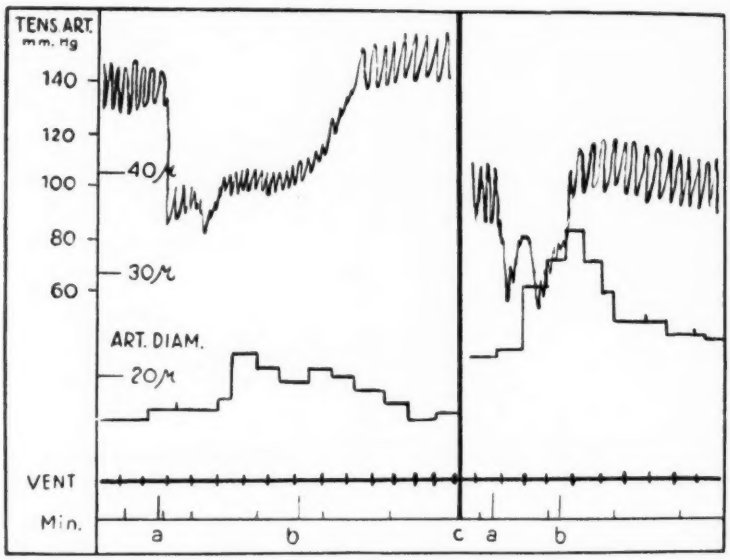

Fig. 7.—Chart showing the difference in the reactions of an artery to a fall in blood pressure from a high and from a low initial tension. The interval from *a* to *b* represents the period of stimulation of the peripheral end of the vagus nerve.

If in the same animals a number of stimulations of the vagus or carotid sinus nerve was performed and the "resting blood pressure" of the animals between these experiments was reduced by bleeding, there was a certain relationship between the amount of fall in the blood pressure and the reaction of the arteries. This brings out clearly that the same percentage of reduction in tension caused far greater vascular dilation in cases in which the initial blood pressure level was low than in those in which it was high. Thus, in figure 7 a fall from 140 to 95 mm. of mercury caused only slight arterial dilation (from 16 to 22 microns), while in the same animal a fall from 110 to 55 mm.

of mercury caused pronounced dilation (from 21 to 35 microns). Thus it appears as though the phenomenon of dilation comes to the fore only when the drop produced in blood pressure signifies danger with regard to the cerebral blood supply.

In the majority of experiments the diameter of the arterioles was seen to decrease during the first thirty or sixty seconds of the fall in blood pressure. The decrease in diameter was slight in comparison with the subsequent dilation. In another paper I shall discuss the question of how this initial arterial constriction is supposed to arise.

In closing I may mention that after removal of the squama occipitalis and parts of the cerebellum in two cats, faradic stimulâtion was

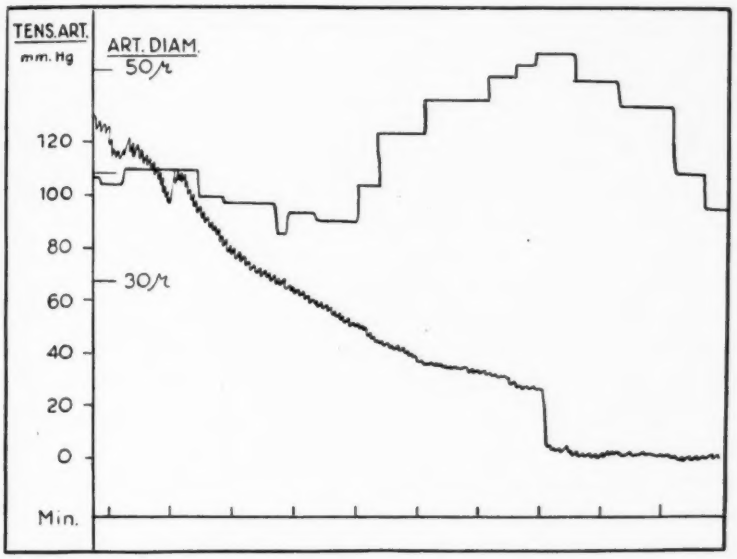

Fig. 8.—The reactions of the pial artery during a spontaneous fall in the blood pressure until the death of the animal.

applied to the motor vagus nucleus in the floor of the fourth ventricle. The reaction of the arteries during the fall in blood pressure thus produced was identical with that previously described.

Figure 8 shows graphically the vascular reactions in an animal which suffered a spontaneous fall in blood pressure until it died. It is seen from the curve that the lumen of the artery decreased slightly with the fall in blood pressure until the latter was about 60 mm. Thereupon the artery dilated and finally, when the blood pressure was less than 10 mm., again constricted. When death occurs, the diameter of the arterioles usually approaches that noted under normal conditions of pressure.

COMMENT

The result of these experiments can be summed up as follows: In by far the majority of cases a fall in arterial tension was followed by an increase in the diameter of the pial arteries. Before this dilation appears slight constriction usually occurs, lasting for from one and a half to two minutes. The vascular reaction seems to be contingent on the reduced endovascular pressure alone, since it takes place independently of whether the fall in tension is due to: (1) stimulation of vasosensory nerves (i. e., peripheral vascular dilation together with limitation of the work of the heart), (2) stimulation of the peripheral end of the vagus nerve (i. e., reduction of the cardiac output alone) or (3) hemorrhage (i. e., a decreased blood volume).

The lower the blood pressure before the fall, the greater the vascular reaction. Within certain limits the dilations are somewhat dependent also on the amount of fall in blood pressure. The vasosensory nerves apparently have no direct influence on this phenomenon of dilation.

These experiments confirm observations made by others [10] (but differently interpreted) that a fall in blood pressure may be associated with expansion of the pial arteries.

Previously, when this reaction to stimulation of the vasosensory nerves was observed, either indirectly (Heymans and Bourckaert [11] or Gollwitzer-Meier and Schulte [12]) or by direct microscopy (Cobb and Finesinger [7] or Ask-Upmark [8]), it was thought to be a direct result of stimulating a nervous pathway which ended in vasodilator fibers on the cerebral arteries. In other words, it was thought that these arteries behaved like vessels in the rest of the body; i. e., they responded to an increased stimulation from the depressor and carotid sinus nerves with dilation. My experiments, however, indicate that the pial arteries react in another way; i. e., they are not subject to the control of the vasosensory nerves. It is rather the variation in the endovascular pressure itself which determines the reactions. The observation that the dilation sets in from one and a half to two minutes after the fall in blood pressure seems to prove that the dilation is not a cause of the fall in blood pressure but a result of it.

One must remember in this connection that a decrease in blood pressure in intact animals effects a decrease in the activity of the vasosensory dilatory nerves and, along with this, a contraction of the

10. Callenfels.[3] Forbes and Wolff.[6] Cobb and Finesinger.[7] Ask-Upmark.[8]

11. Heymans, C., and Bourckaert, J. J.: Compt. rend. Soc. de biol. **100**:202, 1929.

12. Gollwitzer-Meier, K., and Schulte, H.: Arch. f. exper. Path. u. Pharmakol. **165**:685, 1932.

vessels in the regions under their control. Therefore, the dilation of the pial arteries during arterial hypotension cannot be explained as a simple reflex action of the carotid sinus or depressor nerves.

Naturally, the question arises whether the observed expansion of the lumen of the vessel really is of neurogenic origin or whether it arises from another source, i. e., from a decrease in the oxygen tension or an increase in the carbon dioxide tension of the circulating blood (Schmidt;[13] Wolff, Lennox and Allen[14]). This supposition is supported by the fact (1) that the reactions set in after a latent interval which is too long to be typical of nervous action, and (2) that the dilation is especially pronounced when the blood pressure is low; that is to say, when the circulation is greatly threatened.

Various factors, however, argue against this explanation. For example, one never sees a distinct change in the color of the blood. Several experiments were carried out with artificial respiration, and it was seen that the results did not deviate from those obtained with natural respiration. A recording of the normal respiration of several animals did not reveal any respiratory changes during hypotension (fig. 7). Finally, the results of a series of experiments (not yet reported) on the effect of an increase in the blood pressure on the pial arteries argue against the supposition that there is a connection between dilation and the carbon dioxide tension of the blood.

The foregoing experiments did not permit the determination of whether the vascular reactions are caused by special characteristics of the musculature (possibly connected with peripheral ganglion cells of these arterioles) or whether they are due to a definite intracranial reflex mechanism. Cobb and Finesinger's[7] valuable demonstration of dilation of the pial arteries after stimulation of the facial nerve indicates the possible presence of such a reflex mechanism.

I have already stated that in a number of cases the diameter of the artery remained unchanged during a fall in arterial tension (table 1). This must doubtless be interpreted as an "active" tonic regulation of the same type as the reaction of dilation. Unless there is a simultaneous decrease in the constrictor tone of the vessels the lumen should become narrower when the inner pressure decreases.

On the other hand, the initial diminution of the lumen which occurs in almost all cases when there is a sudden drop in blood pressure must undoubtedly be looked on as a "passive" and purely mechanical result of the suddenly reduced endovascular pressure. It is only after a

13. Schmidt, C. F.: Am. J. Physiol. **84**:202, 1928.

14. Wolff, H. G.; Lennox, W. G., and Allen, M. B.: Cerebral Circulation: XII. The Effect on Pial Vessels of Variations in the Oxygen and Carbon Dioxide Content of the Blood, Arch. Neurol. & Psychiat. **23**:1097 (June) 1930.

latent period of from one and a half to two minutes that this "passivity" is supplanted by "active" regulation. The fact that earlier research workers, for instance, Ask-Upmark,[8] found only this "passive" reaction in a considerable number of cases is probably because a sudden fall of blood pressure was produced that did not last for longer than sixty seconds. During a slow fall, constriction does not set in at all (fig. 5).

SUMMARY

The reaction of the pial arteries during a fall in blood pressure was observed in twenty cats. Eighty-nine experiments were made, the blood pressure being reduced by various methods: (*a*) stimulation of the carotid sinus and depressor nerves, (*b*) peripheral stimulation of the vagus nerve and (*c*) arterial and venous hemorrhage.

Regardless of the way in which the arterial hypotension was produced, certain characteristic vasomotor reactions occurred, as follows: There was usually an initial constriction of the lumen of the vessel, which was replaced by distinct dilation after from one and a half to two minutes. The amount of dilation is dependent primarily on the level of the pressure at the beginning of the experiment. The lower the blood pressure, the greater the reaction. During a gradual fall the initial constriction is not seen.

The reactions are independent of the carotid sinus and depressor nerves and of the cervical sympathetic nerves; they take place unchanged even after these nerves have been severed.

The hypothesis is advanced that it is the change in the endovascular pressure in the pial arteries which determines the reaction observed. The mechanism involved in this phenomenon cannot be explained on the basis of the experiments undertaken.

RELATION OF THE CAROTID SINUS TO THE AUTONOMIC NERVOUS SYSTEM AND THE NEUROSES

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Since the pioneer work of Hering [1] in 1926 a mass of experimental data has accumulated concerning the function of the carotid sinus in animals. The significance of the carotid sinus mechanism in man, particularly as regards certain abnormal bodily states, has, however, not been duly appreciated in the United States until recently. One of us (S. W.) and Baker [2] reported the cases of a series of fifteen patients, all of whom complained of attacks of unconsciousness, with or without convulsions, which were caused by a hypersensitive carotid sinus reflex. In a recent publication we [3] reported studies of thirty-two additional patients suffering from syncopal attacks of carotid sinus origin. This syndrome is reflex in nature, and the reflex pathways are parts of the autonomic nervous system. In other reports [4] we

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1. Hering, H. E.: Karotissinusreflexe auf Herz und Gefässe vom normal-physiologischen, pathologisch-physiologischen und klinischen Standpunkt, Dresden, Theodor Steinkopff, 1927.

2. Weiss, Soma, and Baker, J. P.: The Carotid Sinus Reflex in Health and Disease: Its Rôle in the Causation of Fainting and Convulsions, Medicine **12**:297, 1933.

3. Ferris, E. B., Jr.; Capps, R. B., and Weiss, Soma: Carotid Sinus Syncope and Its Bearing on the Mechanism of the Unconscious State and Convulsions: A Study of Thirty-Two Additional Cases, Medicine **14**:377, 1935.

4. (*a*) Weiss, Soma, and Ferris, E. B., Jr.: Adams-Stokes Syndrome with Transient Complete Heart Block of Vagovagal Reflex Origin: Mechanism and Treatment, Arch. Int. Med. **54**:931 (Dec.) 1934. (*b*) Weiss, Soma: Syncope and Related Syndromes, in Christian, H. A., and Mackenzie, J.: Oxford Medicine, New York, Oxford University Press, 1935, vol. 2, p. 9.

presented evidence of the nature of other types of reflex syncope, such as vasovagal, vagovagal and oculocardiac syncope. It seems desirable to bring together the results of these studies in more detail, as well as other more recent observations which throw light on the vegetative nervous system in man, in order to understand better a number of neurogenic manifestations which are commonly encountered and are classified under the general term vegetative neurosis.

Since a detailed review of the literature concerning the carotid sinus both in animals and in man may be found in monographs [5] already published, only a brief discussion of the most significant aspects of the work on this subject will be attempted in the present report.

The nerve endings in the carotid sinus communicate with the medullary centers partly by way of the intercarotid nerve of Hering [1] and to a less extent through sensory fibers along the hypoglossal, glossopharyngeal, vagus and sympathetic nerves.[6] According to many observers, such specialized endings are limited to the carotid sinus and the aortic arch, but Braeucker [7] found similar endings in the walls of other arteries, and Sunder-Plassman,[8] in the walls of the bronchi. There is evidence that certain of these receptor organs are sensitive only to a stretch stimulus, while others respond only to a chemical stimulus. Heymans and Rijlant [9] and others [10] expressed the belief that impulses mediated through chemical stimulation are dependent on the near-by carotid body, whereas stretch impulses pass directly along afferent pathways. Impulses which originate in the carotid sinus pass centrally and connect with many autonomic efferent pathways, the best known

5. Weiss and Baker.[2] Ferris, Capps and Weiss.[3]

6. (*a*) Sunder-Plassman, P.: Untersuchungen über den Bulbus carotidis bei Mensch und Tier im Hinblick auf die "Sinusreflexe" nach H. E. Hering; ein Vergleich mit anderen Gefäss-strecken, die Histopathologie des Bulbus carotidis; das Glomus caroticum, Ztschr. f. d. ges. Anat. (Abt. 1) **93**:567, 1930. (*b*) Braeucker, W.: Neue Untersuchungsergebnisse über das pressorezeptorische Nervensystem und seine praktische Bedeutung in der Chirurgie, Zentralbl. f. Chir. **60**:854, 1933.

7. (*a*) Braeucker, W.: Das pressorezeptorische Nervensystem und seine praktische Bedeutung in der Chirurgie, Beitr. z. klin. Chir. **158**:309, 1933; (*b*) footnote 6b.

8. Sunder-Plassman, P.: Ueber nervöse Receptorenfelder in der Wand der intrapulmonalen Bronchien des Menschen und ihre klinische Bedeutung, insbesondere ihre Shockwirkung bei Lungenoperationen, Deutsche Ztschr. f. Chir. **240**:249, 1933.

9. Heymans, C., and Rijlant, P.: Le courant d'action du nerf du sinus carotidien intact, Compt. rend. Soc. de biol. **113**:69, 1933.

10. Bogue, J. Y., and Stella, G.: Afferent Impulses in the Carotid Sinus Nerve (Nerve of Hering) During Asphyxia and Anoxemia, J. Physiol. **83**:459, 1935.

of which in animals are the pressor and depressor nerves. The systemic blood pressure falls when the sinus is stimulated by increased pressure from within and rises when the intrasinal pressure is decreased. The stimulus results from stretch or relaxation of the receptor organs of the carotid sinus brought about through changing pressure from within the artery. Other common manifestations of stimulation of the carotid sinus in animals are the vagal and the respiratory response. In animals it has been found that the carotid sinus responds to stimulation with a number of chemicals, such as carbon dioxide, potassium cyanide, digitalis, lobeline, nicotine and salicylates.[11] The relation which the carotid sinus bears to the antonomic nervous system in animals has been studied by Hering [1] and by others,[12] who expressed the belief that the carotid sinus exerts a major regulatory influence on the tonus of this system.

The study by one of us and Baker [2] and our previous work [3] have thrown light on the mechanism of the abnormal carotid sinus reflex in man and indirectly on the function of the normal carotid sinus, as well as on the mechanism of the autonomic nervous system. These studies have demonstrated that unconsciousness may be induced by mechanical stimulation of the carotid sinus through one of three mechanisms; thus, the syndrome can be divided into the following types on the basis of changes in the heart rate and blood pressure and the effect of certain drugs on these manifestations during stimulation of the carotid sinus: (1) the vagal type, in which unconsciousness results from cerebral anoxemia due to reflex cardiac asystole; (2) the depressor type, in which fainting results from cerebral anoxemia due to a fall in blood pressure, and (3) the cerebral type, in which unconsciousness occurs without any significant change in the heart rate or blood pressure and there is no alteration in the blood flow through the brain. The chief characteristics of these three types of carotid sinus syncope are outlined in table 1. We have reported the effects of a number of drugs on these types of syncope.[3] These observations have an important bearing on the sympathetic nervous system and will be considered in more detail presently.

11. (*a*) Heymans, C.; Bouckaert, J. J., and Regniers, P.: Le sinus carotidien et la zone homologue cardio-aortique: Physiologie, pharmacologie, pathologie, clinique, Paris, Gaston Doin & Cie, 1933. (*b*) Wright, Samson: The Mode of Action of Certain Drugs Which Stimulate Respiration, J. Pharmacol. & Exper. Therap. **54**:1, 1935. (*c*) Schmidt, C.: Carotid Sinus Reflexes to the Respiratory Center, Am. J. Physiol. **102**:94, 1932.

12. Koch, E.: Die reflektorische Selbststeuerung des Kreislaufes, in Kisch, Bruno: Ergebnisse der Kreislaufforschung, Dresden, Theodor Steinkopff, 1931, vol. 1. Heymans, Bouckaert and Regniers.[11a]

METHOD OF APPROACH

Observations in the present study were made on fifty-six patients exhibiting the carotid sinus syndrome whom we have observed since the beginning of our studies on the carotid sinus three years ago. The method of study was essentially the same as that reported in our previous publication in regard both to diagnosis and to the state of the vegetative nervous system of the patient. Besides observations on the blood pressure, heart rate, color of the skin, gastric motility and changes in the caliber of the pial vessels, we measured changes in the electrical resistance of the skin of the palmar and dorsal surfaces of the hand. The state of the peripheral vessels of the hand and the reflex changes in the caliber of these vessels was studied with a hand plethysmograph before and after denervation of the carotid sinus. The specificity of the carotid sinus reaction has been further demonstrated by the induction of symptoms during ether anesthesia and by suddenly releasing the occluded common carotid artery low in the neck, thereby causing a sudden increase in the intrasinal blood pressure. This procedure was adequately described in a recent study by Gammon.[13] We tested the carotid sinus reaction during the cumulative action of several small doses of sodium cyanide. The effects of nitrites

TABLE 1.—*Three Types of Carotid Sinus Syncope*

Type	Chief Characteristics	
Vagal type, 19 cases	Cardiac asystole Cerebral anoxemia Abolished by atropine, epinephrine or ephedrine Accentuated by digitalis and acetylbetamethylcholine	Combinations of these types
Depressor type, 3 cases	Fall in blood pressure Cerebral anoxemia Abolished by epinephrine and ephedrine Accentuated by nitrites	
Cerebral type, 34 cases	Normal heart rate and blood pressure Normal total cerebral blood flow Not influenced by atropine or epinephrine Accentuated by digitalis and sodium cyanide	

on the depressor type of carotid sinus syncope and of acetylbetamethylcholine on the vagal type was observed. The relation of the carotid sinus to symptoms of respiratory disturbance and to changes in the basal metabolic rate was also studied. The effect of surgical denervation of the carotid sinus on the syncopal attacks has been reported.[14] We studied further the effect of such denervation on a number of autonomic functions of the body, as well as on many functional manifestations unrelated to syncopal attacks which were exhibited by patients in the group on whom operation was performed. Studies were also made on a number of patients suffering from syncopal attacks unrelated to the carotid sinus and from various types of vegetative neuroses.

In order to elucidate the relationship of the carotid sinus and other reflex phenomena to the autonomic nervous system and to the neuroses, the pertinent results of previous studies will be referred to.

13. Gammon, G. D.: The Carotid Sinus Reflex in Patients with Hypertension, J. Clin. Investigation **15**:153, 1936.

14. Weiss, Soma; Capps, R. B.; Ferris, E. B., Jr., and Munro, D.: Syncope and Convulsions Due to a Hyperactive Carotid Sinus Reflex: Diagnosis and Treatment, Arch. Int. Med. **58**:407 (Sept.) 1936.

RESULTS

Of the fifty-six patients, nineteen fainted because of cardiac asystole and three because of a fall in blood pressure, and thirty-four fainted without any significant alteration in the heart rate or blood pressure.

Local Abnormality in the Region of the Carotid Sinus.—As we have previously pointed out, many patients showed evidence of disease in the region of the carotid sinus, such as cervical adenitis and dilatation or sclerosis of the carotid artery. Figure 1 shows the marked atherosclerotic changes present in one member of the group with the vagal type of syncope who subsequently died of an unrelated carcinoma. The close relationship between active tuberculosis of the cervical nodes

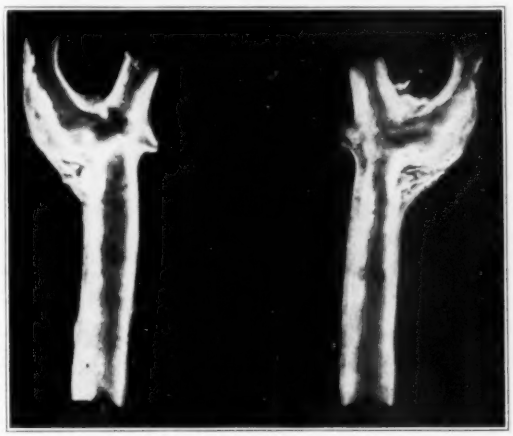

Fig. 1.—Specimen of the left common carotid artery at its bifurcation, obtained at autopsy in one of the cases included in this study. The patient was a woman aged 68 whose attacks were of the vagal type. Marked atherosclerotic thickening of the wall at the bifurcation and a slight amount of atherosclerosis in the arteries distally are shown.

and the sensitivity of the carotid sinus in one case indicates the important rôle which local disease about the sinus may assume in sensitizing this reflex. A normal carotid sinus response, however, has been observed frequently in the presence of such pathologic alterations.

Systemic Disease.—The parallel relationship which exists between sensitivity of the carotid sinus and systemic disease is particularly significant.[3] Subsidence of carotid sinus sensitivity occurred after antisyphilitic therapy in a patient with syphilis of the central nervous system of the meningovascular type.[3] The spinal fluid of this patient contained 40 cells, indicating a fairly active process which might be expected to respond to antisyphilitic therapy. Three patients

with severe dietary deficiency associated with chronic alcoholism also had an abnormal carotid sinus reaction, which disappeared after adequate treatment.[3] In ten patients suffering from acute and chronic alcoholism but without evident dietary deficiency, the carotid sinus response was normal. This observation suggests that the reaction was related to the dietary deficiency rather than to any specific action of alcohol. Reference has already been made to the sensitizing effect of digitalis on both the vagal and the cerebral type of carotid sinus reaction.[14] In five patients symptoms of carotid sinus sensitivity appeared with the onset of the menopause. This observation, together with the previously reported relationship of carotid sinus sensitivity to menstruation,[3] suggests that the glands of internal secretion may be a factor in altering the sensitivity.

Symptoms and Signs Associated with Carotid Sinus Syncope.—As previously described,[3] many of the patients showed various neurotic stigmas, in addition to the symptoms associated with the syncopal attacks, which in themselves would have been regarded as psychogenic had we not been able to find the precipitating cause in the carotid sinus. Six patients showed evidence of a severe vegetative neurosis. Such symptoms as "nervousness," constant fatigue, loss of ambition, mental depression, palpitation of the heart and emotional instability were frequently encountered and occurred independently of the spontaneous and induced syncopal attacks. Symptoms of a functional nature, similar to those which occur in syncopal attacks of varying etiology, were likewise manifested in association with the spontaneous and induced attacks of syncope. In addition to the fainting, dizziness and such premonitory symptoms as numbness and tingling of the extremities, sleepiness, blurring of vision, weakness, amnesia, cataplexy and epigastric distress were complained of.

Objective neurogenic manifestations independent of the syncopal attacks were likewise frequently observed; these included dermatographia, erythema, Raynaud's disease, acrocyanosis, angina pectoris and tremors of the extremities. Symptoms associated with the attacks have been adequately described [5] and include, besides the convulsions, pallor and flushing of the face, hyperpnea, increased gastro-intestinal peristalsis and other less common manifestations. The various symptom complexes most commonly encountered and induced are listed in table 2.

Although pallor of the face usually was characteristic of the group with the cerebral type, in four instances the syncope was accompanied by flushing. In this group the heart rate frequently slowed; in five instances, however, there was no change, and in three the rate actually increased. Alterations of the blood pressure likewise were variable, there being an increase in blood pressure during syncope in two cases.

Hyperpnea accompanied the attacks as a rule, but in in one patient both the spontaneous and the induced attacks were accompanied by a period of complete apnea, which lasted for from one to two minutes. This period of apnea could be induced by mechanical stimulation of the carotid sinus, even during the second stage of ether anesthesia.

Cerebral Blood Flow and State of the Cerebral Blood Vessels.—We have previously demonstrated that the vagal and the depressor type of syncope are brought about by cerebral anoxemia and that in the cerebral type there is no change in the blood flow through the head.[3]

TABLE 2.—*Symptoms Directly Related to the Carotid Sinus Mechanism* *

Carotid sinus	Central	Fainting; dizziness; weakness
		Convulsions (contralateral, bilateral)
		Amnesia; cataplexy
		Sleeplike states
		Fatigue; weakness
	Ocular	Pupillary changes
		Strabismus
		Lacrimation
	Respiratory	Hyperpnea
		Apnea
		Yawning
		Sighing
	Gastro-intestinal	Gaseous eructations
		Nausea; vomiting
		Increased peristalsis
	Vasomotor	Hypotension
		Peripheral constriction
		Peripheral dilatation
		Sweating
	Cardiac	Bradycardia
		Arrhythmia
		Palpitation
	Extremities	Numbness; tingling
		Convulsions
		Babinski phenomenon

* The symptoms and signs recorded in the table accompanied the attacks of unconsciousness brought about by mechanical stimulation of the carotid sinus. All the subjective manifestations were present during the spontaneous attacks.

Through observations on the color of the face and on the spinal fluid, we also demonstrated that constriction of certain cerebral vessels occurs in many patients during syncope but that the tendency to faint does not parallel such changes.[3] From previous studies by Forbes and Wolff [15] and by one of us (S. W.), Robb and Ellis [16] it seems that the pial vessels are the ones involved in this constriction. Since the

15. Forbes, H. S., and Wolff, H. G.: Cerebral Circulation: III. The Vasomotor Control of Cerebral Vessels, Arch. Neurol. & Psychiat. **19**:1057 (June) 1928.

16. Weiss, Soma; Robb, G. P., and Ellis, L. B.: The Systemic Effects of Histamine in Man, with Special Reference to the Responses of the Cardiovascular System, Arch. Int. Med. **49**:360 (March) 1932.

pial vessels probably do not contribute a great deal of blood to the vital centers of the brain itself, the lack of relationship between the caliber of the pial vessels and the cerebral blood flow is more easily understood. These observations are in agreement with those of Bouckaert and Heymans,[17] who were unable to demonstrate a constrictor effect of the carotid sinus on the vessels of the midbrain and the brain stem in animals.

Effect of Drugs.—The effect on the carotid sinus reflex of many drugs which act on the autonomic nervous system has been studied.[5] Atropine, through its action on the vagal endings, prevented the vagal type of syncope but had no influence on the cerebral or the depressor type. Epinephrine and ephedrine, by inducing an independent ventricular rhythm in the presence of auriculoventricular blocks, also prevented the vagal type of syncope. These drugs likewise prevent the depressor type of syncope by abolishing the reflex fall in blood pressure, through their effect on the tone of the peripheral vessels; however, they did not alter the cerebral type. Physostigmine and pilocarpine, which are alleged to stimulate parasympathetic endings, did not enhance the vagal reaction as one might expect.[3] Acetylbetamethylcholine, a powerful vagal stimulant, when administered to a patient with the vagal type, greatly increased the tendency to faint and the degree of auriculoventricular block which could be induced. This drug does not alter the cerebral reaction. Digitalis, through its vagal action, likewise accentuated the vagal reaction. It also enhanced the cerebral reaction, apparently as a result of local action on the carotid sinus, although we were not able to state with certainty that such an effect was not due to its central action.

It has been pointed out that drugs, such as sodium nitrite and amyl nitrite, which lower the blood pressure do not alter the cerebral type of reaction.[3] In a patient recently under observation, who suffered from syncopal attacks due to a combination of the cerebral and the depressor type, a definite increase in the tendency to faint was observed after the administration of these drugs. He was a man aged 59 who had suffered from frequent syncopal attacks during the year prior to examination. The systolic blood pressure was 210 mm. of mercury and the diastolic 120 mm. After atropinization (1 mg., in a solution injected intravenously), pressure over the left carotid sinus induced unconsciousness and convulsions within twenty-five seconds. The systolic blood pressure fell from 195 to 170 mm., a decrease which was considered insufficient to induce unconsciousness. There was no change in the heart rate. The patient then was given several inhalations of

17. Bouckaert, J. J., and Heymans, C.: On the Reflex Regulation of the Cerebral Blood Flow and the Cerebral Vaso-Motor Tone, J. Physiol. **84**:367, 1935.

amyl nitrite; one minute later the systolic blood pressure was 200 mm. Stimulation of the left carotid sinus at this time induced syncope and convulsions in nine seconds, and the systolic blood pressure fell to 130 mm. On another occasion the patient was given 3 grains (0.2 Gm.) of sodium nitrite by mouth. Fifteen minutes later no change in the pulse rate or the blood pressure was noted. Pressure over the left carotid sinus at this time induced syncope in twelve seconds, and the systolic blood pressure fell from 185 to 140 mm. These observations, which were repeated and confirmed on several occasions, show that nitrites enhance the depressor type of reaction, probably by diminishing the tone of the peripheral vessels. One of us (S. W.) and Ellis [18] have shown that nitrites have a similar effect in orthostatic syncope.

Sodium cyanide has been shown specifically to stimulate the carotid sinus to produce hyperpnea.[11b] This reaction has been utilized clinically [19] to determine the pulmonary and the venous circulation time. We have pointed out that sodium cyanide will cause slowing of the heart in patients having the vagal type of carotid sinus reaction and that it will induce symptoms of a mild nature in persons having the cerebral type.[3] Three doses of 0.2 cc. of a 2 per cent solution of sodium cyanide were administered intravenously at intervals of two minutes to a patient who had had syncopal attacks of carotid sinus origin but in whom at the time mechanical stimulation of the carotid sinus did not induce syncope. During the cumulative effect of the drug pressure for fifteen seconds over the right carotid sinus induced syncope. It is assumed that in this case the constant stimulation of the sinus by sodium cyanide, when added to the mechanical stimulation, was sufficient to produce syncope, although neither of the stimuli alone would do so.

Further Evidence That the Carotid Sinus Reflex Was Hyperactive in the Patients Studied.—Our studies [3] demonstrated that in the group of patients with carotid sinus syncope the carotid sinus is abnormally sensitive not only to mechanical but to chemical stimulation, as demonstrated with sodium cyanide, and to the more physiologic stimulation induced by suddenly altering the intrasinal pressure. Since the last report, we have demonstrated repeatedly the last-mentioned fact by occluding the carotid artery below the sinus and suddenly releasing it. The rush of blood into the sinus increases the intrasinal pressure temporarily and thus induces symptoms of a mild nature. The result

18. Weiss, S., and Ellis, L. B.: Influence of Sodium Nitrite on the Cardiovascular System and on Renal Activity in Health, in Arterial Hypertension and in Renal Disease, Arch. Int. Med. **52**:105 (July) 1933. Weiss.[4b]

19. Robb, G. P., and Weiss, S.: A Method for the Measurement of the Velocity of the Pulmonary and Peripheral Venous Blood Flow in Man, Am. Heart J. **8**:650, 1933.

of suddenly increasing the intrasinal pressure is more clearly shown by observations on a patient who suffered from the vagal type of syncope. Pressure over the right carotid sinus induced cardiac standstill for three seconds. While the right carotid artery was occluded well below the sinus with the thumb and then suddenly released, continuous electrocardiographic tracings showed a definite transient slowing of the heart at the moment pressure was released (fig. 2). Observations on six normal patients as a control failed to demonstrate any significant slowing of the heart rate coincident with the release of pressure.

We have also presented considerable evidence that the carotid sinus reaction is not psychogenic.[3] In the case of the patient recently observed who became apneic during pressure on the carotid sinus, the fact that the reaction still occurred while the patient was anesthetized rules out the possibility of a psychogenic origin.

Carotid Sinus Syndromes Other Than Fainting Attacks.—In certain of the patients studied attacks closely related to, but not typical of,

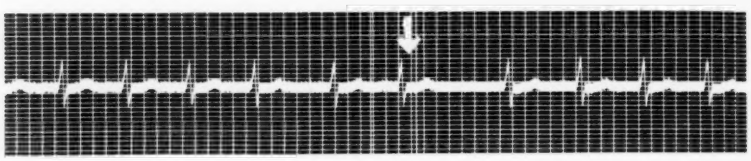

Fig. 2.—Electrocardiogram (lead I) showing slowing of the heart rate induced by suddenly increasing the intrasinal pressure in a patient having the vagal type of syncope. The arrow indicates the time at which the occluded right common carotid artery was released.

ordinary fainting spells occurred. The most remarkable of these attacks were those simulating amnesia, cataplexy and sleep.[3] Another interesting syndrome related to the carotid sinus was observed in a woman aged 56 whose chief complaint was frequent attacks of hyperpnea, associated with dizziness and occasionally with fainting. These attacks occurred more frequently during periods of emotional stress and exacerbation of chronic pulmonary tuberculosis. She was known to have had tuberculosis of the cervical lymph nodes in childhood, and small cervical nodes were palpable on both sides of the neck. Pressure over each carotid sinus induced marked hyperpnea, which lasted for two minutes. When stimulation of the carotid sinus was maintained for twenty seconds or longer, unconsciousness occurred also. This respiratory reaction is somewhat similar to that previously cited in two patients with hypertensive heart disease in whom stimulation of the carotid sinus induced not only fainting but attacks simulating paroxysmal dyspnea.[3] In six patients suffering from attacks of paroxysmal dyspnea due to

failure of the left side of the heart, no dyspnea or hyperpnea could be elicited by stimulation of the carotid sinus. This suggests that the carotid sinus does not play a significant part in the dyspnea associated with cardiac failure. On the contrary, during attacks of cardiac asthma pressure on the carotid sinus may benefit the attack through its vasodepressor mechanism.[19a]

Basal Metabolic Rate.—The basal metabolic rate has been found to be abnormally low in a number of the patients studied by us.[3] We measured the basal metabolic rate at frequent intervals in a majority of the patients suffering from the carotid sinus syndrome and were impressed by the marked fluctuation in level from time to time and by the fact that the rate was lowest in patients with the most evidence of a severe vegetative neurosis. Of nine consecutive patients referred to us because of severe vegetative neuroses but with normal carotid sinus reactions, the basal metabolic rate was subnormal in seven instances. In these patients the metabolic rate fluctuated markedly from time to time. In one patient it varied from —4 to —32 per cent during a period of several months. The average minimum metabolic rate for these seven patients was —19.8 per cent, the highest being —4 per cent and the lowest —32 per cent. The two other patients of the neurosis group had metabolic rates of +2 and +15 per cent. None of the patients with either the carotid sinus syndrome or neurosis showed any clinical evidence of myxedema.

It is of interest that in patients with the carotid sinus syndrome the sinus response remained unaltered after the basal metabolic rate was elevated by the administration of thyroid or dinitrophenol.[3] The unrelated "neurotic" symptoms exhibited by many patients of this group were likewise uninfluenced. Nor did the administration of these drugs to two patients of the neurosis group with low metabolic rates (—25 and —32 per cent) alter the neurogenic manifestations. Our studies of the basal metabolic rate have been confined to determinations of the oxygen consumption under basal conditions, and we have made no effort to determine the total metabolism of the patients. A relatively low oxygen consumption rate appears to be present in many patients suffering from functional disease. Although in most instances the patients showing evidence of severe neuroses exhibited the lowest basal metabolic rate, this was not always the case. From our experience, the basal metabolic rate does not always parallel the severity of symptoms in cases of neuroses, which suggests that changes in oxygen consumption are a concomitant rather than a parallel manifestation of the neuroses. The presence of a low rate in so many patients having stig-

19a. Weiss, S., and Robb, G. P.: The Treatment of Cardiac Asthma (Paroxysmal Nocturnal Dyspnea), M. Clin. N. America **16**:961, 1933.

mas of an abnormal autonomic nervous system suggests, however, that regulation of the oxygen consumption is a function of the autonomic nervous system in man. That this particular manifestation represents a special function of the autonomic nervous system seems likely. Our studies [20] and those of Freeman [21] on the effect of dinitrophenol on human subjects show that the metabolic rate can be elevated to as high as +60 per cent without affecting such autonomic functions as the heart rate and blood pressure, which are so typically altered in cases of hyperthyroidism. This lack of parallelism in the activity of different portions of the autonomic nervous system is in agreement with the work of Patek and one of us (S. W.),[22] who showed that changes in tonus may be limited to portions of rather than to the entire autonomic nervous system.

Electrical Resistance of the Skin.—We have shown that the electrical resistance of the skin of the arms and legs, as roughly estimated by the electrocardiogram, tends to be high.[3] We have since made observations of the electrical resistance of the skin on the dorsum and the palm of the hand. The factors which determine the actual level of cutaneous resistance are not clear at present,[23] nor are the factors which bring about fluctuations in the level of resistance in the dorsum of the hand clearly understood; however, such changes are thought to be related to alterations in tonus of certain portions of the autonomic nervous system. The psychogalvanic reflex, which designates the rapid fall in the palmar cutaneous resistance brought about by painful or nerve stimuli, has been shown to be due to increased sympathetic tonus.[24] The dorsal cutaneous resistance of the hand was found to be high in the group of patients with carotid sinus syncope, as compared with that of persons used as controls. The palmar resistance appeared to be within the limits of the normal. The psychogalvanic response likewise was similar to that seen in normal persons, except in one patient, in whom it was absent. Since this patient had combined system disease and postural hypotension, as well as the carotid sinus syndrome, the absence of the psychogalvanic response was considered to be caused

20. Ferris, E. B., Jr.: Unpublished observations. Robb and Weiss.[19]

21. Freeman, H.: The Effect of Dinitrophenol upon the Circulation Time, J. Pharmacol. & Exper. Therap. **51**:477, 1934.

22. Patek, A., and Weiss, S.: The Tonus of the Autonomic Nervous System in Arterial Hypertension, New England J. Med. **205**:330, 1931.

23. Solomon, Philip: The Psychogalvanic Reflex: Applications to Neurology and Psychiatry, Arch. Neurol. & Psychiat. **34**:818 (Oct.) 1935.

24. Richter, C. P.: Physiological Factors Involved in the Electrical Resistance of the Skin, Am. J. Physiol. **88**:596, 1929. Richter, C. P., and Shaw, M. B.: Complete Transections of the Spinal Cord at Different Levels: Their Effect on Sweating, Arch. Neurol. & Psychiat. **24**:1107 (Dec.) 1930.

by a lesion of the spinal cord involving the sympathetic system rather than by the abnormal carotid sinus reflex or any general alteration in sympathetic tonus.

SURGICAL DENERVATION OF THE CAROTID SINUS

Effect on Syncope.—The curative effect of surgical denervation of the carotid sinus in ten patients suffering from carotid sinus syncope has been adequately discussed.[14] Of the ten patients on whom operation was performed, eight remained free from syncopal attacks.

Effect on Certain Functions of the Autonomic Nervous System.—Subjective Manifestations: Definite improvement of certain symptoms occurred immediately after recovery from denervation of the sinus, particularly in patients who suffered from severe vasomotor instability. Four patients independently volunteered the information that after operation visual acuity improved. They could see objects more distinctly, and colors and light seemed brighter. They also experienced a feeling of well-being and increased vigor, and there was a corresponding disappearance of the constant fatigue which is frequently experienced by patients with neuroses. Because of the relief of such symptoms following operation, it was thought at first that they might have been causally related to the hypersensitive carotid sinus reflex; however, within from a few days to a few weeks after the operation these subjective sensations returned to their original state, although the syncopal attacks were permanently relieved. Except for the many functional symptoms associated with the attacks of syncope, none of the other symptoms in patients having neuroses was permanently influenced by the operation, and there was no improvement in the patients' general emotional state.

Heart Rate and Blood Pressure: Figure 3 shows the transient effect of operation on the heart rate and blood pressure of a patient in the group on whom operation was performed. It has already been pointed out that the rise in heart rate and blood pressure which immediately follows section of the sinus nerve is only temporary.[3]

Tone of the Peripheral Vessels: Studies of the blood flow in the hands of two of the patients by means of a plethysmograph demonstrated that no significant change from the normal had occurred in the blood flow in the hand several days after operation. Reflex vasoconstriction of the small vessels of the hand induced by painful stimuli (the pinch reflex [25]) occurred to a normal degree. Reflex vasodilation

25. Capps, R. B.: A Method for Measuring Tone and Reflex Constriction of the Capillaries, Venules and Veins of the Human Hand with the Results in Normal and Diseased States, J. Clin. Investigation **15**:229, 1936.

of these vessels induced by heating the blood (the Landis test [26]) was likewise normal after the operation.

Basal Metabolic Rate: The basal metabolic rates of three patients before and after operation are shown in table 3. We noted no permanent increase in the basal metabolic rate of such patients over a prolonged period. There was a transient rise in the metabolism of one patient immediately after operation, an observation which may or may not be significant.

Resistance of the Skin: In three of the group on whom operation was performed no significant change was noted either in the palmar or the dorsal resistance of the hand or in the psychogalvanic response.

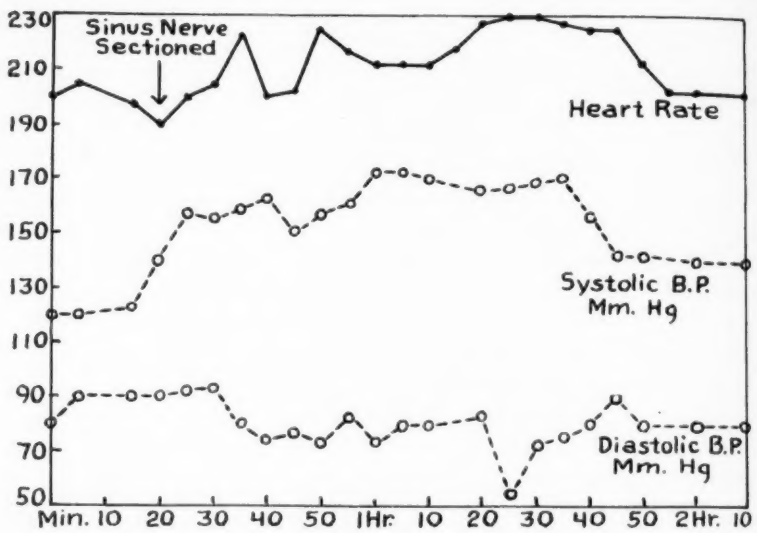

Fig. 3.—Record of the heart rate and blood pressure during surgical denervation of the carotid sinus in a patient (case 5) with the cerebral type of syncope. The systolic blood pressure tends to rise, and the diastolic remains essentially unchanged. The heart rate and blood pressure returned almost to their normal levels within two hours. The curve for the heart rate represents variations from 80 to 136 beats per minute.

Raynaud's Disease: Since the publication of our previous studies, we have encountered an unusual case of Raynaud's syndrome in a patient suffering also from the cerebral type of carotid sinus syncope. An Irish housewife aged 46, in addition to having symptoms related to the syncopal attacks and to a definite vegetative neurosis, complained that from time to time small areas of pallor, from 2 to 20 mm. in diam-

26. Landis, E. M., Jr.: Vasodilatation in the Lower Extremities in Response to Immersing the Forearms in Warm Water, J. Clin. Investigation **11**:1019, 1932.

eter, appeared over the skin of her arms. The location of these areas varied widely at different times. The presence of such areas of pallor was confirmed by one of us on three occasions. The frequency of these attacks did not abate after denervation of the carotid sinus. On the contrary, they became more frequent, and soon the fingers became involved. Three months after operation, the patient had almost continuous attacks of pallor, numbness and tingling of the fingers with associated cyanosis, typical of Raynaud's disease. At no time could these attacks be related to exposure to cold. The symptoms reached their maximum severity during July and August, the warmest months of the year. It appears likely that Raynaud's disease in this patient was neurogenic. The persistence of the attacks of Raynaud's disease after operation, together with the fact that the symptoms related to

TABLE 3.—*Basal Metabolic Rates Taken at Varying Intervals in Three Patients with the Cerebral Type of Syncope* *

Patient J. D.		Patient R. R.		Patient W. B.	
Date	Metabolic Rate, Percentage	Date	Metabolic Rate, Percentage	Date	Metabolic Rate, Percentage
11/ 8/33	—19				
11/20/33	—20	11/28/33	—10	1/28/35	—20
11/24/33	—25	12/ 1/33	— 9	2/ 1/35	—26
11/29/33	—11	12/ 4/33	— 8	2/ 4/35	—19
1/11/34	Sinus Denervated	12/12/33	Sinus Denervated	2/11/35	Sinus Denervated
1/22/34	+ 4	12/19/33	—11	2/16/35	—13
1/24/34	+ 7	1/ 3/34	— 8	2/23/35	—14
2/23/34	—14				
3/ 2/35	—11				

* Fluctuations in level are shown. The definite rise following operation in J. D. was only temporary and is of questionable significance.

the carotid sinus were entirely relieved, demonstrates the lack of relationship in this patient between Raynaud's disease and the hyperactive carotid sinus reflex.

Angina Pectoris: Although we have previously reported the occurrence of angina pectoris with the carotid sinus syndrome, it seems worth while to report the case of a patient recently under observation who suffered from this combination of symptoms, for the anginal attacks seemed to be neurogenic. The attacks of angina pectoris in this patient were typical as to both the type and radiation of pain and the response to nitrites. They were, however, related in no way to exertion; in fact, they often occurred during periods of rest in bed. The onset of attacks appeared to be more frequently associated with periods of emotional stress. Denervation of the carotid sinus did not in any way influence these attacks, and they occurred as frequently after as before the operation.

COMMENT

We have shown the definite relationship between the carotid sinus mechanism and the spontaneous attacks of syncope and related manifestations in patients in whom the carotid sinus is sensitive to mechanical stimulation. The demonstration of an abnormal vagal response to increased intrasinal pressure in a patient of the vagal type and the enhancement of the reaction by the administration of sodium cyanide are further evidences of the specificity of this reaction and demonstrate that in such patients the carotid sinus is sensitive not only to mechanical but to chemical stimulation, and to stimulation from intrasinal pressure as well.

The various manifestations, listed in table 2, which may be induced by stimulation of the carotid sinus, indicate the widespread efferent autonomic pathways through which a stimulus from one sensory area may pass. These pathways include, among others, the vagus and the respiratory nerves and the vasomotor nerves to the blood vessels of the face, pia-arachnoid and hand. The fact that effects opposed to those usually seen in association with the carotid sinus syndrome, namely, apnea, tachycardia, increase in blood pressure and dilatation of the vessels of the face and hands, have been observed in a small group of patients indicates that impulses from the carotid sinus may in one patient stimulate and in another inhibit similar autonomic functions. That the impulses may pass centrally and alter the tonus of certain vegetative centers also seems likely, in view of the group of central manifestations, such as unconsciousness, cataplexy and narcolepsy, which have been brought about by stimulation of the carotid sinus in the absence of cerebral ischemia, and in view of the evidence that no alteration in cerebral blood flow occurs in the cerebral type of syncope.[5] It is of significance that these pathways fall largely in the autonomic nervous system and that symptoms of identical nature are encountered in various other types of syncope and vegetative neuroses. We have previously pointed out the relative frequency with which a local pathologic condition in the region of the carotid sinus has been encountered. The frequent presence of hypertension in the depressor group and of heart disease in the vagal group [5] also indicates the importance of pathologic changes in the efferent side of the reflex arc, as does the enhancement of the depressor reaction by nitrites and of the vagal reaction by acetylbetamethylcholine and digitalis. The only drugs which alter the symptoms of the carotid sinus syndrome are those which act on portions of the efferent pathway of the reflex, namely, atropine, digitalis and acetylbetamethylcholine, in the vagal type, and ephedrine, epinephrine and nitrites, in the depressor type. It is also significant that we have been unable to find any nonhabit-forming drug capable of altering

the central or sensory portion of this reflex, with the exception of digitalis and sodium cyanide, which sensitize it. A similar situation exists regarding the action of drugs on many manifestations of neuroses. The carotid sinus reflex offers an excellent opportunity to test the action of drugs on the central and the motor portion of the autonomic nervous system. Thus, in selected patients various types of autonomic response can be induced at will by means of mechanical stimulation of the carotid sinus, and the influence of drugs on such responses can be determined.

Effect of the Carotid Sinus on the Tonus of the Autonomic Nervous System.—Stimulation of the hypersensitive carotid sinuses of these patients brought about widespread manifestations through various autonomic efferent pathways, such as the vagus, the vasodepressor, the vasoconstrictor and the respiratory nerves. There can be no question but that the afferent pathways to the carotid sinus are intimately connected both with the various autonomic centers in the brain and with various efferent pathways.

The temporary alteration of the pulse and blood pressure and the transient improvement in subjective sensations immediately after operation suggest that the carotid sinus may play a part in maintaining autonomic tonus. Our results, however, do not bear out the contention that the carotid sinus exerts a major influence in regulating autonomic tonus as a whole as suggested by Hering.[26a] The manifestations present during each attack were absent between the attacks. Identical manifestations caused by other reflex mechanisms, such as oculocardiac, vagovagal, vasovagal and orthostatic syncope, could not be reproduced by stimulation of the carotid sinus in patients suffering from such syndromes.[27] Many manifestations of a functional nature such as Raynaud's syndrome, angina pectoris, a low basal metabolic rate, dermatographia and chronic fatigue, could not be permanently altered either by stimulation or by denervation of the carotid sinus. The facts that the changes in the blood pressure and the pulse which occurred during denervation of the carotid sinus were temporary and that after denervation vascular reflexes in the hand were shown to be normal also suggest that in these patients the sensitive carotid sinus had little constant influence on sympathetic and parasympathetic tonus. Other work on animals has corroborated these conclusions. It has been shown that permanent changes in the blood pressure cannot be induced merely by denervating both carotid sinuses. Heymans and his associates [11a]

26a. Hering, H. E.: Der Blutdruckzüglertonus in seiner Bedeutung für den Parasympathikustonus und Sympathikustonus, Leipzig, Georg Thieme, 1932.

27. Ferris, Capps and Weiss.[3] Weiss and Ferris.[4]

and others [28] stated that, in addition to cutting the carotid sinus nerves, it is necessary to cut the two aortic depressor nerves in order to produce permanent hypertension in animals. Green and De Groat,[29] however, showed that even when both the carotid sinus and the aortic depressor nerves are cut, the blood pressure will eventually return to its normal level. The studies of Braeucker [30] and of Sunder-Plassman [31] are further evidence that the carotid sinus is only one of a number of sensory areas in the body which may influence the tonus of the autonomic nervous system. When the influence of the carotid sinus is removed by surgical denervation, the normal tonus is soon taken over and maintained by other portions of the autonomic nervous system.

Clinical Concept of the Reflex Mechanism of Various Symptom Complexes.—The results of this study and of previous studies show that the carotid sinus is only one of a number of sensory stations from which symptoms of an identical nature may be produced. There are many examples of such sensory mechanisms. Two of us (S. W. and E. B. F. Jr.[4a]) reported a case of vagovagal syncope in which impulses originating in a diverticulum of the esophagus reflexly caused sufficient vagal stimulation to produce cardiac standstill. Reflex depression of the blood pressure also occurred in this patient. We reported other cases in which a similar vagal reflex was set up in the bronchi, the pharynx, the larynx and the eyeball. Capps and Lewis [32] cited instances in which vagal and depressor reflexes could be induced by pleural irritation.

The frequency with which local abnormalities about the sensitive carotid sinus were observed in the patients studied in this report suggests that in most cases the hypersensitive carotid sinus reflex resulted from a pathologic or a physiologic change in the sinus. In addition, we have presented evidence that diseases involving the motor side of the reflex (cardiac and vascular disease) or of the central synapses (disease of the spinal cord) may also be factors in conditioning such a reflex.[3] That organic disease may play an important rôle in other neurogenic syndromes having similar manifestations is also evident. The patients cited by us [4a] who suffered from various types of reflex syncope

28. Nowak, S. J. G.: Personal communication.

29. Green, M. F., and De Groat, A.: Observations on Late Effects of Denervation of Carotid Sinuses and Section of Depressor Nerves, Am. J. Physiol. **112**:488, 1935.

30. Braeucker: Footnotes *6b* and *7a*.

31. Sunder-Plassman: Footnotes *6a* and 8.

32. Capps, J. A., and Lewis, D. D.: Observations upon Certain Blood Pressure Lowering Reflexes That Arise from Irritation of the Inflamed Pleura, Tr. A. Am. Physicians **22**:635, 1907; Blood Pressure Lowering Reflexes from Irritation of the Chest in Empyema, ibid. **23**:188, 1908.

showed morphologic changes in the area where the sensory impulses originated, namely, in the esophagus, the pharynx, the trachea and bronchi and the eye. The relation of head injury to epilepsy is well known. The reflex effects of arteriovenous aneurysm on the heart rate and blood pressure, which were studied by Ellis and one of us (S. W.),[33] also suggest the influence of local injury in sensitizing sensory endings, and the studies of pleural reflexes in animals by Capps and Lewis [32] bore this out. The latter authors could obtain marked vagal and depressor reactions when the pleura had been previously injured but were unable to elicit any reaction when the normal pleura was stimulated. Thus, it appears that organic disease may be a factor in conditioning reflex pathways and, hence, in determining the type of symptomatology in certain neurogenic conditions; likewise, injury in many potential areas of the body may alter the excitability of sensory endings present in such areas, so that a given stimulus which is without effect under physiologic conditions may under such abnormal conditions bring forth a sensory response.

We have indicated that the carotid sinus reaction may be altered in certain patients by emotional states [3] and also by factors associated with the menopause and with menstruation. A similar relationship between the severity of manifestations in organic disease and these emotional factors is well known clinically. Thus, in some apparently functional conditions in which the symptoms are altered by psychic influences but no anatomic cause can be observed, the emotional state of the patient may not be necessarily the primary cause.

The studies presented demonstrate that many objective and subjective clinical manifestations of the autonomic nervous system may be induced by sensory impulses from many areas of the body. These sensory impulses may stimulate a vegetative function in one patient and depress the same function in another. The similarity of these signs and symptoms to those encountered in association with many hitherto unexplained vasomotor or vegetative neuroses not only implies a common efferent reflex mechanism but suggests that in some of these neuroses an anatomic abnormality may be the primary cause of the symptoms. Structural damage cannot necessarily be ruled out in a patient simply because his symptoms can be influenced by psychogenic factors. Although we do not wish to minimize the important rôle assumed by the emotions either in neuroses or in organic disease, we believe that the importance of morphologic changes is sometimes underestimated in certain vegetative or "vasomotor" neuroses. The knowledge of the mechanism of the autonomic nervous system which may be obtained

33. Ellis, L. B., and Weiss, S.: The Local and Systemic Effects of Arterio-Venous Fistula on the Circulation in Man, Am. Heart J. **5**:635, 1930.

by studies of such abnormal reflex states in man may lead to a better understanding of the neuroses and to a more rational therapeutic approach.

CONCLUSIONS

1. Studies of fifty-six patients suffering from the carotid sinus syndrome are reported.

2. Although a temporary alteration in the tonus of the autonomic nervous system may follow denervation of the hypersensitive carotid sinus, no permanent change in vegetative functions occurs other than the manifestations directly associated with the carotid sinus syndrome.

3. Surgical denervation of the carotid sinus does not alter the symptoms in patients having vegetative neuroses.

4. The administration of small doses of sodium cyanide increases the sensitivity of the carotid sinus to mechanical stimulation.

5. By acting on the peripheral vascular system, nitrites greatly accentuate the depressor reaction of the carotid sinus.

6. Impulses from the carotid sinus may induce manifestations opposite in nature in different persons.

7. The relation of local and systemic disease to the carotid sinus reflex and other abnormal autonomic reflexes has been stressed.

8. The basal metabolic rate is frequently subnormal in patients suffering from various types of neuroses. Our observations suggest that oxygen consumption is a function of the autonomic nervous system and is not necessarily an indication of thyroid activity.

9. Such areas as the eyeball, pharynx, larynx, bronchus, pleura and esophagus and arteriovenous aneurysms have been cited as recognized examples of sensory stations which under abnormal conditions can influence certain efferent portions of the autonomic nervous system in the same manner as the abnormal carotid sinus.

10. These studies suggest that organic disease may play a much greater rôle in the mechanism of many vegetative neuroses than is generally thought.

11. Patients suffering from the carotid sinus syndrome present an excellent opportunity to study certain portions of the reflex pathways involved in various types of neuroses.

12. The carotid sinus does not appear to play a major rôle in regulating the constant tonus of the autonomic nervous system.

Technical and Occasional Notes

EXTIRPATION OF A HUGE PINEALOMA FROM A PATIENT WITH PUBERTAS PRAECOX: A NEW OPERATIVE APPROACH

GILBERT HORRAX, M.D., BOSTON

Since the early unsuccessful attempts to remove pineal tumors by Brunner (quoted by Rorschach [1]) in 1913 and by Puussep [2] in 1914, operative approach to these deeply seated, yet often relatively benign, growths has been by two main routes. The first of these was described in great detail by Dandy.[3] By this method the pineal region is exposed from above by separating the posterior portion of one cerebral hemisphere from its venous attachments to the sagittal sinus, retracting the hemisphere outward and then incising the caudal end of the corpus callosum (fig. 1). The second method is that described by Van Wagenen.[4] This consists in a transventricular exposure of the area in question by an incision through the right occipital region down to the posterior part of the dilated right lateral ventricle, after which the medial wall of the ventricle is incised and the growth disclosed (fig. 2).

By one or the other of these methods not only Dandy and Van Wagenen but Foerster,[5] Sachs [6] and Harris and Cairns [7] reported the successful removal of pineal tumors. Although his article was published in 1928, Foerster performed operation on his two patients in 1923 and 1927, respectively. He used a slight modification of the method described by Dandy in that the occipital lobe was retracted upward and outward, away from the tentorium and falx. From the patient on whom he operated in 1923 Foerster removed 10 cc. of cystic fluid and a portion of the wall of the cyst. This patient remained in

From the Neurological Service of the Lahey Clinic and the New England Deaconess Hospital.

Read by title at the Sixty-Second Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 3, 1936.

1. Rorschach, H.: Zur Pathologie und Operabilität der Tumoren der Zirbeldrüse, Beitr. z. klin. Chir. **83**:451, 1913.

2. Puussep, L.: Das operative Entfernung einer Zyste der Glandula pinealis, Neurol. Centralbl. **33**:560, 1914.

3. Dandy, W. E.: An Operation for the Removal of Pineal Tumors, Surg., Gynec. & Obst. **33**:113, 1921.

4. Van Wagenen, W. P.: A Surgical Approach for the Removal of Certain Pineal Tumors, Surg., Gynec. & Obst. **53**:216, 1931.

5. Foerster, O.: Das operative Vorgehen bei Tumoren der Vierhügelgegend. Wien. klin. Wchnschr. **41**:986, 1928.

6. Sachs, E.: Diagnosis and Treatment of Brain Tumors, St. Louis, C. V. Mosby Company, 1931.

7. Harris, W., and Cairns, H. W. B.: Diagnosis and Treatment of Pineal Tumors, Lancet **1**:3, 1932.

relatively good health for from six to seven months, when pressure symptoms recurred and death took place three days after a second puncture of the cyst. In Foerster's other case he observed a solid tumor

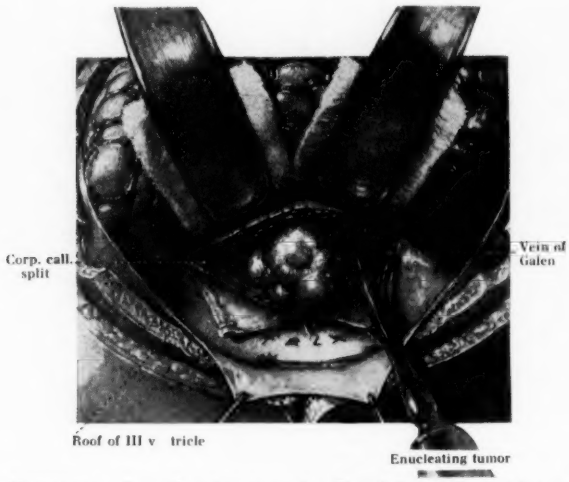

Fig. 1.—Exposure of a pineal tumor by Dandy's method (from Dandy [3]).

Fig. 2.—Transventricular exposure of a pineal tumor (from Van Wagenen [4]).

the "size of a large prune." This growth was apparently completely removed piecemeal, and the patient was in excellent condition five months later, except that he was nearly blind. At the time Van Wagenen and

Harris and Cairns published their articles, the patients had survived, respectively, fifteen and thirteen months after operation. The patient of Harris and Cairns showed signs of recurrence of the tumor nine months after the growth was removed but improved with roentgen therapy. Dandy's patient survived eight months, and Sachs' patient, from whom an unclassified cyst of the pineal region was removed, was well and active five years later. In addition to these reported cases, Dr. W. J. German, of the New Haven Hospital, sent me in a personal communication the records of two patients from whom he removed a pineal tumor. These operations were performed in 1930 and 1935, respectively, and in both instances the transventricular approach was employed. One patient survived three and one-half months, and the other succumbed in six days. It is probable that both tumors should be classed as pinealoma, although one was termed "astrocytoma of the pineal gland."

In June 1935 [8] I reported at the Sixty-First Annual Meeting of the American Neurological Association the successful removal of a soft pinealoma by the transventricular approach. The patient is alive and well at the time of writing, two and one-half years subsequent to the operation. At this same meeting I reported the case of an adolescent boy who presented the clinical picture of a pineal tumor with the syndrome of pubertas praecox. At that time the growth had not been verified histologically, as only decompression followed by roentgen treatment, which was directed toward the pineal region, had been performed. To this type of therapy he responded exceedingly well for approximately a year, but pressure symptoms reappeared and were not influenced by further irradiation.

It was therefore necessary to attempt operative removal of the tumor. This was accomplished successfully by a two stage procedure. Because of the huge size of the growth, it became evident that the right occipital lobe and a portion of the posterior parietal area would have to be resected in order to expose the encapsulated mass sufficiently to allow its extirpation. By this means an excellent view of the pineal region was obtained, whereas by either of the usual approaches it would have been impossible to obtain an adequate exposure. Since this method may at times become the procedure of choice, a description of the circumstances and the two stage operation seems warranted. It is also of interest to report the case now as another instance of a histologically verified pinealoma in a boy who showed the clinical picture of pubertas praecox.

In regard to operative considerations, the simpler methods of Dandy and Van Wagenen are, of course, preferable for the ordinary, relatively small growths in the pineal region. Van Wagenen stated that the soft mass in his case was about 3 by 3.5 cm. in diameter. In the case of Harris and Cairns the tumor measured 2.8 by 2.3 by 2.2 cm. and weighed 8.75 Gm. In Dandy's surviving patient the tumor (a tuberculoma) measured 5 by 4 cm. His second patient had a larger growth; as nearly as can be made out from the illustrations, it measured approximately 5.5 by 4 by 3.5 cm. It weighed 26 Gm. Conceivably, this growth might have been removed, with survival of the patient, if the occipital lobe had been excised, but it must be remembered that Dandy's procedure

8. Horrax, G.: Further Observations on Tumor of the Pineal Body, Arch. Neurol. & Psychiat. **35**:215 (Feb.) 1936.

was described in 1921 and at that time the idea of resecting a lobe for such a purpose could hardly have been entertained.

The patient for whom it was necessary to resort to this radical excision had the largest pinealoma that has ever come to my attention; so far as I am aware it was considerably larger than any similar growth examined at operation or necropsy. Its measurements were 8 by 4.5 by 3 cm., and its weight was 70 Gm.

The history and neurologic findings in the case have been described in detail in a former contribution;[8] so it will suffice in this paper to give only the salient features.

REPORT OF A CASE

History.—A boy aged 10 years, who had been referred by Dr. G. W. Ewing of Peabody, Mass., to the neurosurgical service of the Lahey Clinic on May 2,

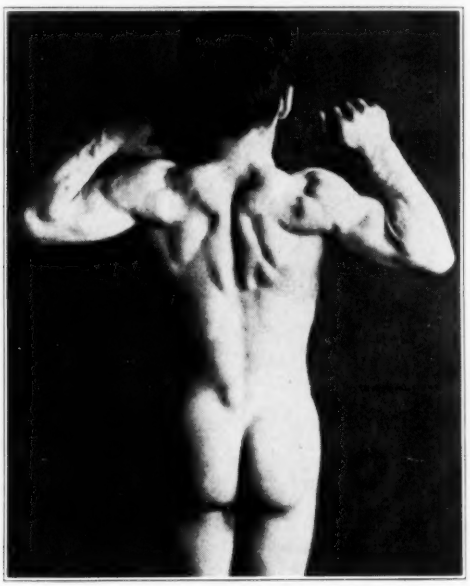

Fig. 3.—Photograph of the patient before operation or roentgen treatment, showing the high degree of muscular development.

1934, was admitted to the New England Deaconess Hospital, complaining of headache and double vision. In addition to the acute symptoms, he gave a history of having grown markedly both in height and in weight during the previous year, becoming extraordinarily muscular, with an increase in facial, body and pubic hair. His appearance in this respect was that of an adult (fig. 3). His voice had "changed," and the external genitalia had reached adult proportions.

Physical and Neurologic Examination.—Examination disclosed the features just described, as well as weakness of the right abducens nerve and bilateral choking of the disks of from 3 to 4 diopters.

Diagnosis.—The presence of a pineal tumor was, of course, almost certain, and this diagnosis was confirmed by a ventriculogram made on May 12, which showed a mass bulging into the posterior portion of the distended third ventricle

and, in addition, greatly dilated lateral ventricles (fig. 4). At this time the child's parents permitted only decompression, followed by roentgen treatment. The first procedure was carried out, therefore, on the same date as the ventriculography, and subsequent radiation was given for six days, starting on May 25. To this therapy the boy responded remarkably well for six months, when pressure symptoms recurred and the head was again irradiated. A third series of roentgen treatments became necessary in April 1935, but from these no relief was obtained. It was now obvious to the parents that a radical attempt to remove the tumor was the only possible course.

First Stage Operation (May 9).—At the time of the original decompression an osteoplastic flap had been outlined, in anticipation of the present operation. This flap was therefore turned down over the occipitoparietal region and the corre-

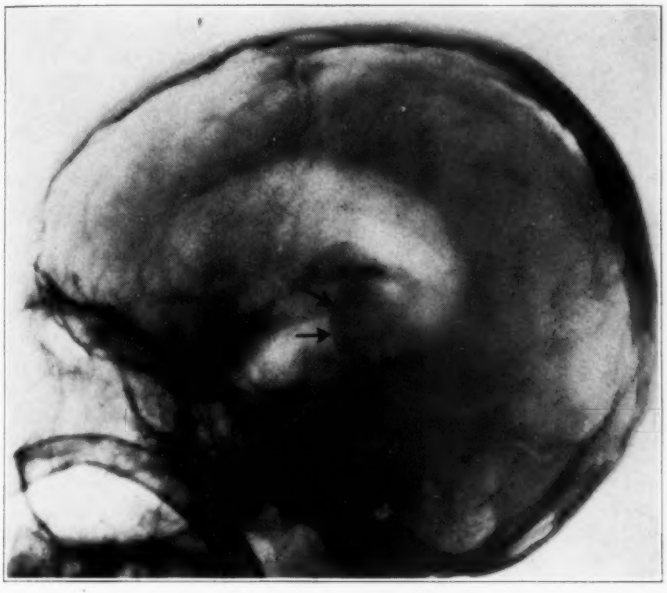

Fig. 4.—Ventriculogram showing dilatation of the lateral ventricles and the shadow of the tumor bulging into the posterior half of the distended third ventricle (indicated by arrows; from Horrax [8]).

sponding posterior area of cortex exposed by reflecting the dura downward and forward. As a preliminary measure, all venous connections between the occipitoparietal cortex and the longitudinal sinus were coagulated and divided. A vertical, transcortical incision was next made down to the greatly dilated lateral ventricle, and by retracting the walls of this incision the bulging floor of the ventricle was disclosed. It was obvious that a tumor lay just below; the medial ventricular wall was therefore incised, and an encapsulated growth presented itself almost immediately (fig. 5). The tumor was exposed more fully by extending the ventricular incision and was observed to be of such large size that it could not be attacked radically with the exposure which it was possible to obtain by retraction of the brain. A large block of the parieto-occipital area was therefore removed posterior to the original cortical incision, thus exposing the falx and corpus callosum for

a considerable area, together with the tentorium posteriorly. With this additional room the anterior margin of the growth could be identified and its capsule also followed backward to where the lesser veins of Galen ran over it. The right lesser vein of Galen was coagulated and divided. Gradually, the anterior two thirds of the mass could be separated from the surrounding structures, but this process was time consuming because of the great vascularity. The operation had already taken several hours, so that it was decided to postpone final enucleation for a second session. However, a piece of growth was removed for histologic examination before the incision was closed. The patient was given a small blood transfusion (300 cc.) from his father the following day.

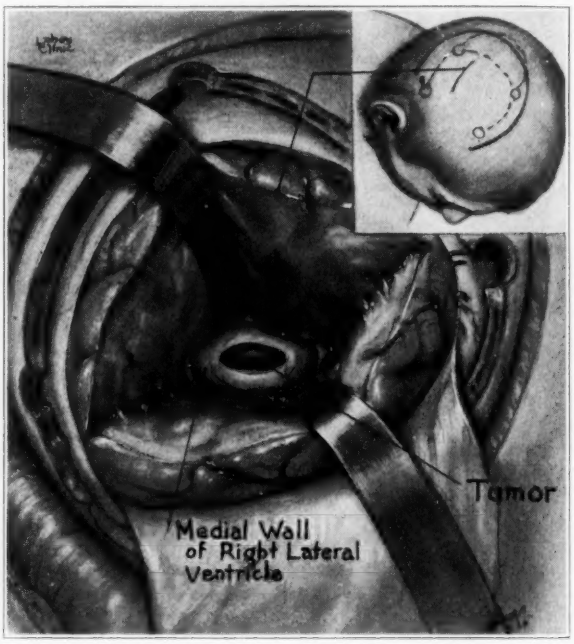

Fig. 5.—Exposure of the tumor by transcortical and transventricular incisions. The insert indicates the relative positions of the bone flap and the cortical incision.

Second Stage Operation (May 17).—On this occasion the operative area was readily exposed by turning down the old bone flap. The small remaining portion of the occipital pole, which had been left at the previous session, was excised. An attempt was then made to extirpate some of the growth inside its capsule in order to reduce its size, but this proved to be impossible because of the extreme vascularity. The tumor proved sufficiently firm, however, so that several silk traction sutures could be taken through it. By lifting up on these the growth was gradually freed well anteriorly, medially and laterally, but in so doing it became necessary to incise the falx upward to gain further room. The left lesser vein of Galen was coagulated. At the posterior pole it was observed that there was a considerable projection of tumor beneath the tentorium, and this portion was liberated finally by splitting the tentorium downward for a distance of 2 or 3 cm. (figs. 6 and 7). The cerebellum could be seen compressed below this projection. As a final

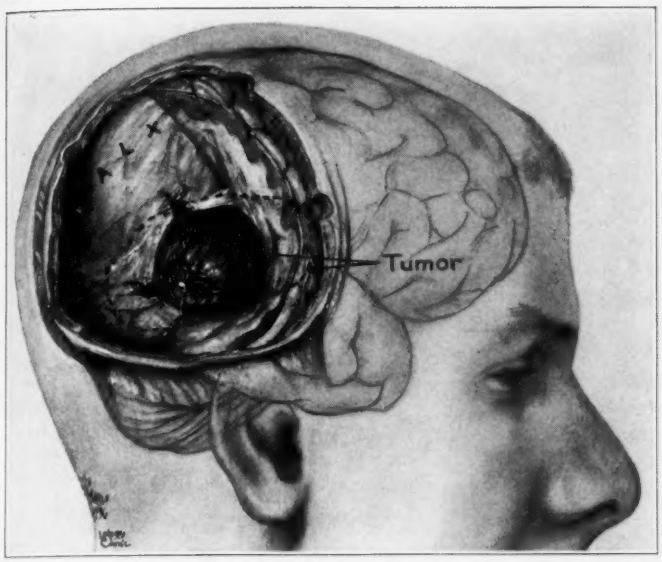

Fig. 6.—Complete exposure of the pineal tumor, with a general view of the region, showing the relationship of the bone flap and excised area to the skull and brain as a whole. The occipital lobe and a portion of the posterior parietal and temporal areas have been resected. The dotted line shows the extent of the unexposed tumor.

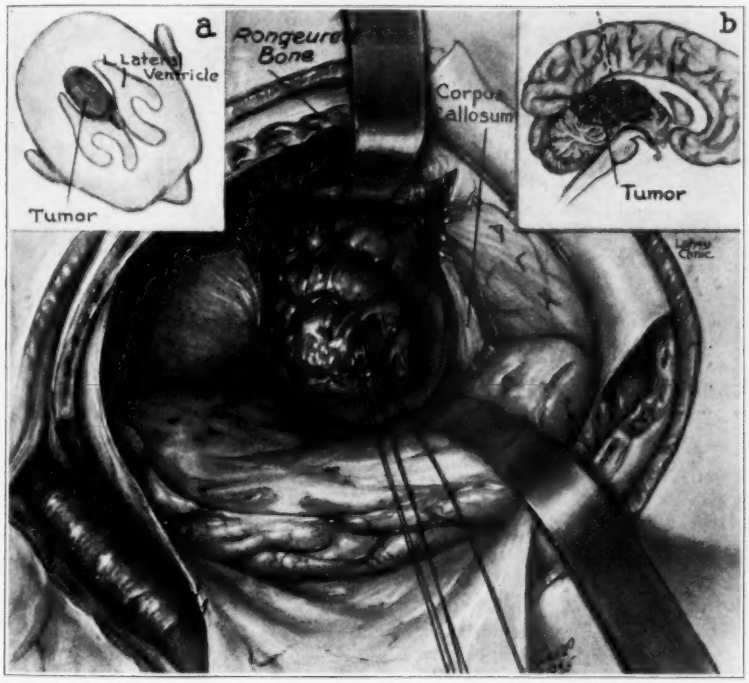

Fig. 7.—Complete exposure of the pineal tumor, illustrating a detail of the procedure shown in figure 6. The right occipital lobe and a portion of the adjacent postparietal and temporal areas have been excised. The falx and tentorium have been incised, and the posterior end of the corpus callosum has been divided. Traction sutures of silk have been placed in the tumor in order that it may be lifted up and dissected free on all sides. The inserts show the relative position and size of the tumor from the lateral and the superior aspect of the brain.

step, the cerebral peduncles were gently separated from the tumor on either side, and the mass was then lifted off the corpora quadrigemina and adjacent portion of the midbrain.

After all places of oozing had been controlled, the large cavity was filled with physiologic solution of sodium chloride, the dura resutured over the upper portion of the field and the lower area left open for purposes of decompression. The flap was replaced and closure carried out with fine silk in layers, without drainage. The operation had taken five and one-half hours, but the child was in fair condition and did not need a transfusion.

Postoperative Course.—The day following operation the patient's temperature rose to 104.5 F. by rectum, and he did not respond. The head and eyes were turned toward the left. The left arm and leg were completely paralyzed, with the deep reflexes exaggerated on this side as compared with those on the right. Babinski's

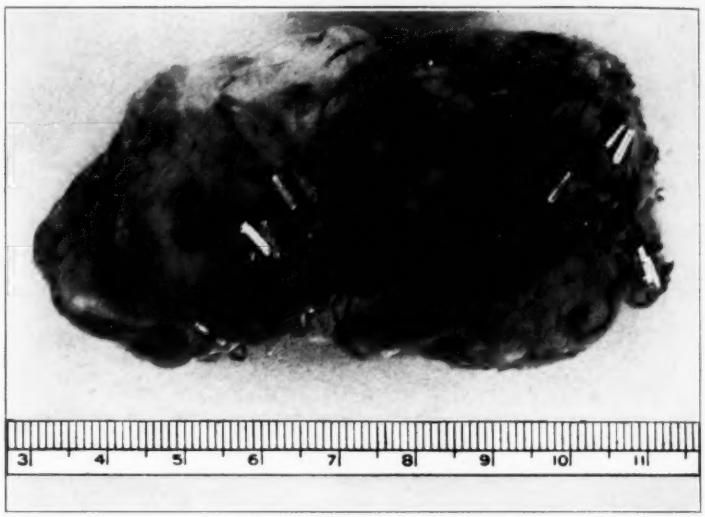

Fig. 8.—Photograph of the tumor removed at operation. (The scale below is in centimeters.)

sign was present bilaterally. The abdominal reflexes were present on the right and absent on the left.

The cavity at the site of operation was tapped daily, and the child gradually improved. On the fourth day after operation he was conscious and rational; he answered questions slowly but accurately and counted fingers correctly. It could be demonstrated that he had complete left homonymous hemianopia. The left pupil was larger than the right, and neither pupil reacted to light. The eyes deviated almost constantly to the left but occasionally returned to the median position and remained there for short periods.

During the course of the next three weeks the patient's neurologic status improved definitely but gradually. He still had marked weakness of the lower part of the face on the left, and the left arm and leg, but the strength on this side was becoming progressively better. Although at first he was unable to move his eyes to the right beyond the median line, it was noted on June 13 that voluntary lateral movements of the eyeballs were complete in both directions. On this date it

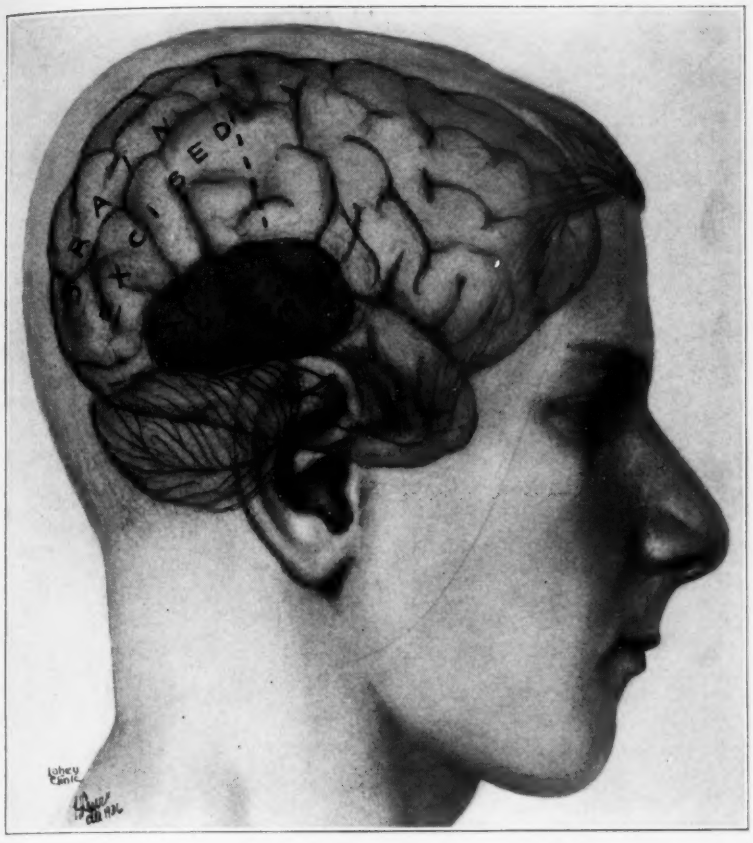

Fig. 9.—Diagrammatic sketch drawn to scale, in order to show the relations of the tumor from the lateral aspect to the approximate area of resection of the lobe.

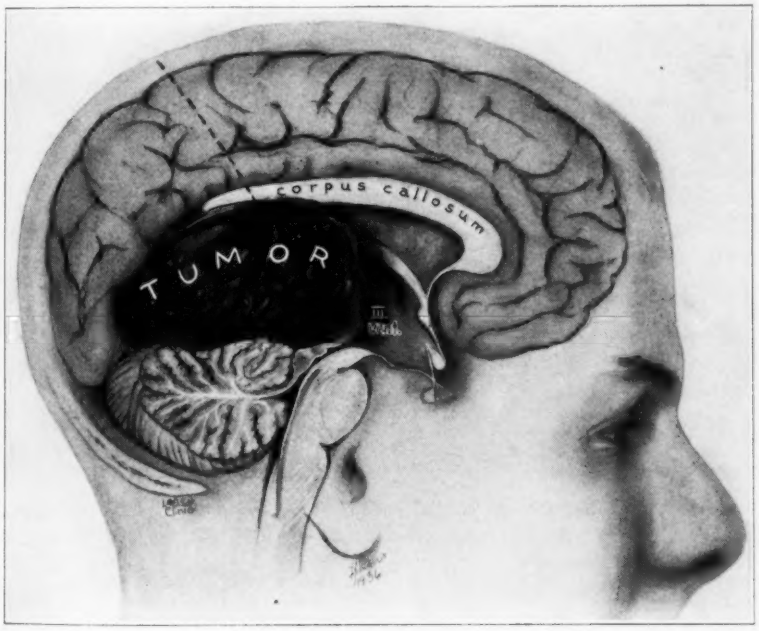

Fig. 10.—Diagrammatic sketch, drawn to scale, to show the approximate relationship of the tumor in a sagittal section.

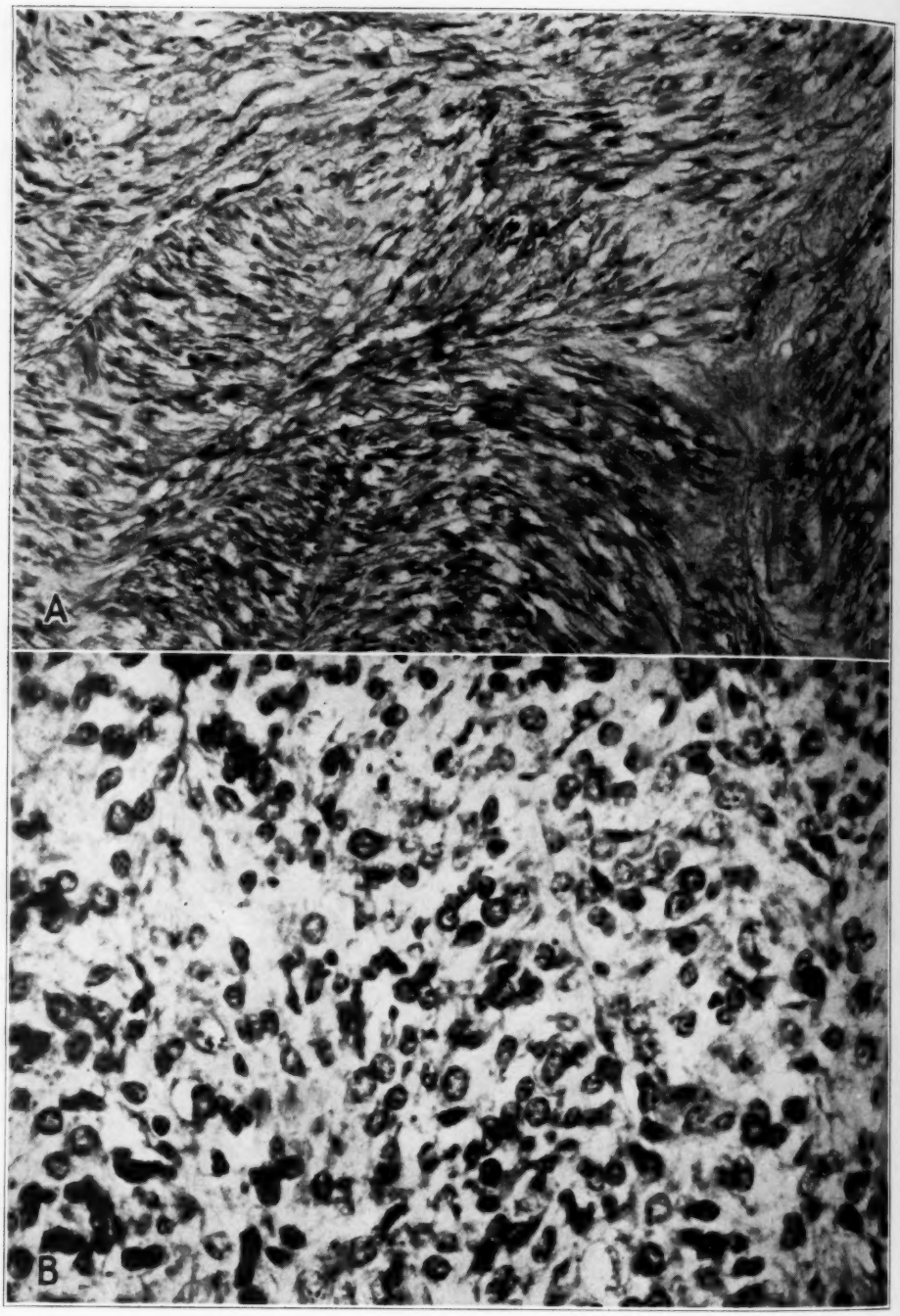

Fig. 11.—Photomicrographs of the tumor showing (*A*) (× 150) the general arrangement of the cells, and (*B*) (× 800) an area of round pineal parenchyma cells of the usual type.

was also observed that the pupils were small (1 mm.) and apparently equal but did not react to light. The size of the pupils was in striking contrast to that in the earlier part of the postoperative period, when they were rather dilated but failed to react to light.

On July 3, seven weeks after operation, another review of the patient's neurologic condition was made. He showed about the same mental status as that

Fig. 12.—Photomicrograph (× 800) of the tumor showing arrangement of the cells of the predominant fusiform type.

previously noted. He was incontinent of urine and feces, this having been the case during the whole postoperative course. He was losing weight, and it was with great difficulty that he could be made to eat at all adequately.

Ocular movements on this date were unrestricted, including conjugate movement upward. The hemiparesis on the left was further improved, but the left arm

and leg were distinctly spastic. The deep reflexes were greater on the left than on the right, including positive Babinski, Oppenheim and Gordon signs and a sustained ankle clonus on the left. There was less response to pinprick and deep muscle pain on the left side. All resistive movements were purposive and well coordinated. The patient was up in a wheel-chair from time to time and finally was discharged to his home on July 17, two months after the final operation.

During the next month he showed little or no gain in any way. He died on August 15, probably of postoperative adhesions which caused a cerebrospinal fluid block. Permission for postmortem examination was not obtained.

Pathologic Observations.—The actual size and shape of the tumor are shown in figure 8, while its size and position with relation to those of neighboring structures are represented in figures 9 and 10. The growth was nodular, firm and extremely vascular, measuring 8 by 4.5 by 3 cm. Its weight, not including that of a few small portions which were removed by the electrosurgical loop, was 70 Gm.

Microscopically the tumor was composed of typical pineal parenchyma cells, largely fusiform and having little cytoplasm. The nuclei were ovoid or slightly lobulated and had a thin nuclear membrane (fig. 11 *A* and *B*). Mitoses were present in moderate numbers. For the most part the cells were arranged in bands, and in some places the cell bodies were long (fig. 12). In occasional cells of this type the striae characteristic of skeletal muscle were recognized. Infiltration of the connective tissue by small round cells was present in only a few areas.

COMMENT

Since the patient from whom this pineal tumor was removed survived the operation only three months, the procedure can by no means be classed as highly successful. Furthermore, the degree of disability which he showed as a result of the operation at least brings up the question as to how radical one should be in attacking a growth of this size in such a situation. As to the first of these points, it may be said that the experience is not related from the standpoint of what might be termed a successful operation. The fact, however, that the patient lived as long as he did after the final operation was a matter of no little surprise.

Concerning the second point, if the size of the growth could have been foretold and the postoperative status predicted more or less accurately, it is doubtful whether any one would have wished such a procedure to be carried out. It is, however, precisely these points which cannot always be prophesied, and it is difficult, if not impossible, to refuse operative intervention in the presence of an otherwise hopeless condition.

The experience is valuable, however, from several aspects. It has demonstrated that a pinealoma of extremely large size may remain encapsulated and be capable of removal surgically. In some instances, with a large tumor of this region it may be necessary to resect a considerable portion of the occipitoparietal area of the right hemisphere in order to secure an exposure which is adequate. Indeed, with some pineal tumors which are much smaller than the one described in this paper, preliminary occipital lobectomy may be wise not only for exposure but to prevent undue retraction, which might be even more damaging to the surrounding area. Such a resection, of course, commits the patient to permanent left homonymous hemianopia and, doubtless, to permanent

changes in the sensory sphere involving the left side. The hemianopic defect, however, was permanent in the patients of both Harris and Cairns and Van Wagenen, and operation was performed by the simpler methods to which reference has been made. Whether this postoperative feature can ever be avoided is therefore uncertain, but in any event it is compatible with a useful life. The same may be said in regard to the sensory changes which were likewise present and apparently permanent in the patient of Harris and Cairns, i. e., impairment of postural sensibility and astereognosis. In the patient whose case is reported in this paper there were, in addition to visual and sensory disturbances, marked motor weakness of the left side and a mental status which, for want of a better term, may be said to have been extremely sluggish. I think, however, that under more favorable circumstances, particularly the opportunity of attacking a similar growth of somewhat smaller dimensions, a patient would recover from these last-mentioned disabilities, as they in no sense resulted from resection of the brain area per se.

Finally, it is not to be intimated in any statement in this paper that there is something new or original in the removal of large areas of the brain, either cerebral or cerebellar, for the exposure of deeply seated tumors. Such resections have been advocated and used by many neurosurgeons for various growths in other situations. Up to the present, however, it does not appear that the method has been applied for the exposure of pineal tumors.

SUMMARY

The extirpation of a pinealoma weighing 70 Gm. from a child showing the clinical syndrome of pubertas praecox is reported. Owing to the unusual size of the growth, a more radical means of exposing the pineal region was employed than has been described previously. It is suggested that this type of exposure may be the procedure of choice for many of the larger growths in this area.

Obituary

FRANKWOOD E. WILLIAMS, M.D.

1883-1936

Frankwood E. Williams, the son of a physician, was born in Cardington, Ohio, in 1883. About the time of his graduation from the University of Wisconsin, in 1907, his father died, and he spent one year teaching in a military school. He graduated in medicine at the University of Michigan in 1912 and served one year at the State Psychopathic Hospital, under the late Dr. A. M. Barrett. He then went as executive officer of the Boston Psychopathic Hospital, under the leadership of the late Dr. E. E. Southard, and after two years became medical director of the Massachusetts Society for Mental Hygiene. In 1917 he went to the National Committee for Mental Hygiene, where he initiated and developed *Mental Hygiene* and supervised other publications of that committee.

During the World War Dr. Williams was commissioned as major in the Army Medical Corps and served first as assistant and later as chief of the Division of Neurology and Psychiatry in the office of the Surgeon General.

Returning to the National Committee for Mental Hygiene after the war, Dr. Williams played an important part in the development of psychiatric social work. The care and treatment of ex-service men whose problems were complicated by their mental attitudes was the occasion for the development of a school of social service at Smith College, where Dr. Williams lectured from 1921 to 1926. Later he taught in the New York School of Social Work and the New School for Social Research.

After the death of Dr. Thomas W. Salmon a decision was required regarding the position of medical director of the National Committee for Mental Hygiene, and after some deliberation Dr. Williams accepted this post, which he held from 1922 to 1931. The work of the organization was expanding into many fields, and some of its best contributions were due to Dr. Williams' vision. He planned the scientific program of the International Congress on Mental Hygiene and edited its proceedings.

Dr. Williams was much in demand as a speaker. Always informed and clear, he could discourse interestingly on any topic in his field, and when addressing himself to some phase of mental health in which wrongs were to be righted and neglect was to be replaced by service, his direct and vigorous sincerity in developing the truth of his theme

fixed the attention of his audience and swept them to his conclusions. His appointments included lectures at Yale University School of Medicine and Columbia University College of Physicians and Surgeons. Colgate University made him a Doctor of Science.

In 1931, after having been psychoanalyzed, Dr. Williams entered private practice, devoting himself largely to psychoanalysis. In this as in his other labors, he was not especially interested in financial questions. Many of his patients were college students. His generosity, particularly to students, was known only by his intimate friends; wherever he went he was on the best of terms with the young.

Dr. Williams was highly conscientious and honorable. His earnest, logical acceptance of what he deemed to be the implications of a truth sometimes brought his opinions into conflict with those of men cast in a different mold. Sometimes his keen and searching criticism of current practice in psychiatry was resented by those who put a different estimate on it. He spoke frankly and wrote cogently, but his antagonism was directed not toward individual persons but toward sets of ideas. He was a consistent liberal. He appreciated art and particularly enjoyed music; in later years he found time to develop his power of expression in that art. He never seemed strong but seldom complained of ill health and was able to undertake heavy programs of writing, travel and speaking without detriment.

Russia attracted his earnest observation. He made several summer trips to that country and was deeply impressed by the humanitarian aspects of its political reorganization. In lectures and articles he set forth effectively his points of admiration. Dr. Williams died on a voyage returning from Russia.

American psychiatry had in Dr. Williams a keen thinker along lines of social betterment. Although actively interested in the individual person he became best known as an exponent of mental health and mental treatment through public agencies. He accomplished much, though he passed away at the age of 53. Probably his contributions to psychiatric integration in the fields of education and social service will stand longest.

SAMUEL W. HAMILTON, M.D.

Abstracts from Current Literature

Anatomy and Embryology

THE DEVELOPMENT AND MORPHOLOGY OF THE CEREBELLUM IN THE OPOSSUM. O. LARSELL, J. Comp. Neurol. **63**:65 (Dec.) 1935; **63**:251 (Feb.) 1936.

Over thirty stages of embryos were available for these studies, as well as pouch young and adults. Part I of the paper describes the development of the cerebellum from its first appearance in the embryo to the beginning of fissuration in the corpus cerebelli. Part II describes the development of the fissures and the subdivisions of the cerebellum and the details of its internal structure in pouch young and in adults.

The first indication of the cerebellum in the opossum appears early on the eleventh day of development. Late on the eleventh day two commissures are distinctly shown. Late on the twelfth day there are a bilaterally symmetrical, massive corpus cerebelli and a flocculonodular lobe. The commissura cerebelli is formed by direct trigeminal fibers, to which the spinocerebellar fibers are added. The corpus cerebelli develops into the principal portion of the mammalian cerebellum and so overshadows the flocculonodular lobe as to obscure its morphologic significance in the adult.

A rapid period of growth of the cerebellum begins at birth, as seen in increased cellular proliferation. As growth of the cerebellum continues and the entering fiber tracts are augmented by additional fibers, the cerebellar base becomes increasingly difficult to analyze. The principal feature of cerebellar development in the pouch young is the great growth of the corpus cerebelli, resulting in foliation of the cortex and formation of fissures. The paraflocculus is formed as a lateral extension of the uvula and the pyramis, with both of which it retains a peduncular connection in the adult. The cortex is organized into the three typical layers. The growth of the three great cerebellar peduncles through the cerebellar base does not have the effect in the adult opossum of separating the deep cerebellar region so completely from the brain stem as in higher mammals.

The corpus cerebelli receives trigeminal, spinocerebellar and tectocerebellar fibers, in addition to secondary vestibular fibers to its more basal parts. The flocculonodular lobe receives primary and secondary vestibular fibers.

The flocculonodular lobe and the corpus cerebelli are the fundamental cerebellar divisions morphologically and probably functionally. The corpus cerebelli is looked on by Larsell as the projection center for muscle sense stimuli and the flocculonodular lobe as the corresponding center for vestibular stimuli.

ADDISON, Philadelphia.

STUDIES ON NEUROGLIA IN MAN. V. TRONCONI, Riv. di pat. nerv. **45**:224 (March-April) 1935.

Tronconi devotes his study to the normal distribution of glial elements in the various layers of the first five cortical fields of von Economo and to the morphologic appearance of glia cells in the brains of persons suffering from general diseases not involving primarily the nerve tissue. He concludes that the microglia and oligodendroglia cells and astrocytes are variously scattered throughout the cortex in the areas mentioned and present only slight differences from layer to layer and from field to field. Such differences are not important enough to establish microscopic characteristics for each of the cortical fields, and, therefore, recognition of a field cannot be based on the distribution of the glial elements.

As a result of his investigation of morphologic changes in the glial elements in association with general systemic diseases, Tronconi advises extreme caution in the evaluation of the pathologic changes in the glia. He reports various types of progressive or regressive changes in apparently normal brains. Gliosis was observed in these cases.

FERRARO, New York.

NEUROVEGETATIVE RECEPTOR FIELDS IN THE MECHANISM OF CIRCULATORY REGULATION AND EXPERIMENTAL PRODUCTION OF MORPHOLOGIC CHANGES IN THE SYMPATHETIC NERVOUS SYSTEM BY THEIR EXCLUSION: NORMAL PRESENCE OF TWO NUCLEI IN THE SYMPATHETIC GANGLION CELLS. KURT HARTING, Ztschr. f. d. ges. Neurol. u. Psychiat. **152**:611 (April) 1935.

Harting criticizes the recent work of Sunder-Plassmann in which the depressor nerve in the rabbit was cut and enlarged binucleate ganglion cells were observed in the sympathetic ganglia. Sunder-Plassmann believed that these ganglion cells were abnormal and showed evidence of degeneration secondary to cutting the autonomic nerves. Harting states that the morphologic characteristics of the ganglion cells described in the work of Sunder-Plassmann are those of the normal sympathetic ganglia of the rabbit. The sympathetic ganglia in man have a different structure. It is therefore erroneous to draw any conclusions about the sympathetic ganglia in man from experimental work on rabbits.

Remak in 1837 pointed out a difference in the nuclei of the sympathetic ganglion cells and those of the spinal ganglion cells. Lubimoff in 1874 noted binucleate ganglion cells in lower animals. Matsui observed 892 binucleate forms in 1,000 sympathetic cells in the rabbit and no binucleate cell in 5,000 cells in the rat or in 63,000 cells of two completely studied superior cervical ganglia in man. Harting studied the superior cervical and the superior celiac ganglia of healthy rabbits and observed only binucleate cells, which Sunder-Plassmann described as distinctly abnormal. He emphasizes the value of accurate knowledge of the normal comparative anatomic and histologic structure before conclusions are drawn from experimental researches

SAVITSKY, New York.

Psychiatry and Psychopathology

LOCAL RESPONSIBILITY FOR A MENTAL HYGIENE PROGRAM. ELLEN C. POTTER, Ment. Hyg. **19**:196 (April) 1935.

To promote good mental health the work of the state should be supplemented by local activities in each community. Three types of decentralized activity are thus possible: (1) provision of methods for educating children and adults, including extension of the social resources useful in promoting good social adjustment; (2) provision of local clinic and institutional facilities for the care and treatment of neurotic and maladjusted persons, and (3) active local supervision of paroled patients. As an illustration of the possibilities, Potter analyzes the economic results of paroling all parolable patients with psychoses living in a single county in New Jersey. She shows that the services of a psychiatric worker and assistant would cost less than the expense of maintaining these patients in the state institution. To effect this, she suggests that the efforts of municipal, county and private agencies be combined under the supervision of an unsalaried, nonpolitical county board to carry out local measures for mental hygiene.

DAVIDSON, Newark, N. J.

THE SUMMER CAMP AS A BEHAVIOR CLINIC. ROBERT L. AMSDEN, Ment. Hyg. **20**:262 (April) 1936.

Camp Onawama, Long Lake, Fenton, Mich., although superficially like other camps, is a behavior clinic conducting experiments in leadership and control, procedures in the adjustment of behavior, and direct approach in the rebuilding of attitudes and personality. In reconstructing the behavior of socially maladjusted boys, delinquent and potentially psychotic, the aim is to interpret behavior rather than to judge it, in order to find a socially acceptable way of providing for each child his unsatisfied "wants."

Each boy presents a separate problem, but usual procedures include working out a tentative plan for every camper, establishing his confidence and talking over

difficulties to help the boy see facts in their relative values. Direct counseling, indirect treatment, as exemplified in the development of a sense of responsibility through opportunities for leadership, giving of awards and punishments and the use of group approval as a means of social control are usually effective means of forming desirable habits. A large group of boys who had been delinquents before attending Camp Onawama had satisfactory school records the following year. A large proportion of the boys at the camp were no longer problem children when placed in a wholesome environment.

The unusually receptive and cooperative attitude of boys while at camp and their opportunities for intimate association with counselors and directors having fine personalities combine to make a summer camp a desirable locus for a behavior clinic.

DAVIDSON, Newark, N. J.

IS DEMENTIA PRAECOX OF TUBERCULOUS ORIGIN? F. D'HOLLANDER and ROUVROY, Ann. méd.-psychol. **90**:417 (Nov., pt. 2) 1932.

D'Hollander and Rouvroy review their work for two years with the injection into guinea-pigs of cerebrospinal fluid from twelve patients with dementia praecox. From 5 to 8 cc. of cerebrospinal fluid was injected subcutaneously into seventy-three animals. Lesions considered to be of typical tuberculous origin were obtained with fluid from eleven of the twelve patients. Two of the twelve patients died of proved tuberculosis within the time of the experiment, and an additional patient died of marasmus, but permission for autopsy was refused. All twelve patients had previously been under observation in the hospital for a prolonged period, with classic dementia praecox.

After injection of the fluid of four other patients the typical acid-fast bacillus of Koch was demonstrated in sections of the inoculated animals. Cultures of the blood of nine of the twelve patients were made, in one third of which tubercule bacilli were found by Löwenstein of Vienna.

The authors review briefly the work of other investigators and note that the observations were positive for tuberculosis in only seven of forty-seven cases. In their conclusions they do not claim to have shown that in all cases of dementia praecox the tubercle bacillus is an etiologic factor, but leave that question for decision after the study of a much larger series of cases. They state, however, that in all of nine cases of dementia praecox in which autopsy was performed they observed chronic meningo-encephalitis resembling an atypical form of tuberculous meningitis. They further ask whether the presence of the virus of tuberculosis in the cerebrospinal fluid is not indisputable proof of the tuberculous origin of the dementia praecox.

MOORE, Boston.

PSYCHOSIS ASSOCIATED WITH GRIP. C. I. URECHIA, Ann. méd.-psychol. **91**:455 (April, pt. 1) 1933.

In great epidemics of grip (1890-1891 and 1918-1919) many nervous affections were noted coincident with the disease or as sequelae. In a recent epidemic in France (1931) a number of cases of psychosis were seen. Twenty cases are described. There is a similarity between the etiologic agent and the epidemic incidence of grip and those of encephalitis. The duration of the psychosis is variable, from a few days to a year. In few cases does the condition become chronic, but there may be some residual signs until recovery is complete. Death may intervene from pulmonary complications or myocarditis.

Postmortem examination shows that the brain is often congested, resulting sometimes in meningeal hemorrhage, or the brain may be anemic and pale. Microscopically there are degenerative alterations; nothing pathognomonic is seen. In rare cases there are slight, discrete inflammatory lesions. Pupillary changes are seen, and these vary from day to day; there is decreased reaction to light,

but never fixation. The cerebrospinal fluid is normal. The urine may contain albumin and, rarely, sugar. Occasionally there are symptoms of meningitis. The mental symptoms consist of confusion, hypochondria, mania and excitement.

MOORE, Boston.

RÔLE OF INSTINCT IN THE PATHOGENESIS OF PSYCHOPATHIC CONDITIONS. DIDE and BARRÈRE, Ann. méd.-psychol. **92**:1 (June, pt. 2) 1934.

A new classification of mental disease is suggested. Manic-depressive psychosis, systematic delirium (interpretative or hallucinatory) and hebephrenic and catatonic syndromes are grouped together as being derived from instability of instinct or, to use the authors' phraseology, "deviation from or insufficiency of instinct." Secondary to the disorders of instinct are the mental symptoms associated with this group. This subclass includes flight of ideas, perceptive or psychomotor hallucinations, indifference, inactivity, suggestibility and the like.

MOORE, Boston.

MELANCHOLIA IN A PERSON WITH ATHEROMA, NORMAL CEREBRAL ARTERIAL TENSION AND PATCHES OF NEUROGLIA. C. I. URECHIA and N. ELEKES, Ann. méd.-psychol. **92**:215 (July, pt. 2) 1934.

Urechia and Elekes report the clinicopathologic changes in the case of a man who died at 68. He had been an inveterate smoker and after financial difficulties had been agitated and anxious and had threatened suicide. The chief pathologic observation was the presence of islands of neuroglia, thought to be due to local irritation. Areas in the neuroglial islands showed partial destruction of cells.

MOORE, Boston.

PSYCHOSIS ACCOMPANYING ACUTE HEMORRHAGIC ENCEPHALITIS. L. MARCHAND and A. COURTOIS, Ann. méd.-psychol. **92**:359 (Oct., pt. 2) 1934.

The cortical and subcortical areas are most often affected in acute hemorrhagic encephalitis. The condition is secondary to thrombosis of small meningeal veins, and is built up by the accumulation of a number of perivenous and pericapillary hemorrhages, causing eventual softening of the surrounding tissue. Clinically, acute delirium occurs, followed by rapidly progressive coma and signs of localization of the lesion (hemiplegia and convulsive attacks). Death ensues rapidly. There is retention of nitrogen in the blood, and the cerebrospinal fluid becomes xanthochromic. It is important to differentiate encephalitis of this type from that which accompanies infectious disease in both children and adults.

MOORE, Boston.

TEST OF PRACTICAL INTELLIGENCE IN CHILDREN. M. LAMBERCIER and A. REY, Arch. de psychol. **25**:1, 1935.

The behavior of children in a practical situation is studied through their attempts to secure a piece of candy fixed to one end of an iron rod suspended out of reach and procurable only through a roundabout method. Toward the middle of the rod is a U-shaped bend. As the rod hangs horizontally this bend is within the child's reach. By pulling on this and manipulating the rod properly he can secure the candy. The group used for the main test consisted of about eighty children, aged from 4 to 8 years, otherwise not described by the authors. The responses made by these children are differentiated into various groups, the most important of which are: (1) attempts to reach the candy directly, a method persisted in by about a fourth of the children and adopted at first but given up readily by another fourth, and (2) attacks on the U-shaped bend, a method characteristic of another fourth of the children and, in general, more characteristic of the older children. Lambercier and Rey discuss in detail the evolution of practical intelligence, as it is shown by this test, from a neuromuscular level to the higher level at which the motor possibilities of the body are realized, the direct route to the goal is inhibited and a roundabout route is substituted.

MCBRIDE, Philadelphia.

Diseases of the Brain

BROMIDE INTOXICATION. T. S. CLAIBORNE, New England J. Med. **212**:1214 (June 27) 1935.

The sydrome of bromide intoxication is encountered frequently in general practice. Acneform eruption and mental lethargy are the most common symptoms but may be accompanied by others to confuse the clinical picture and simulate more serious disease. The history is of little value, since the patient is usually confused. The diagnosis can be verified by the detection of bromide in the urine and blood by the technic of Wuth. The concentration of bromide varies, but normally none is seen in either fluid. Treatment consists in stopping medication with bromides and administering large amounts of sodium chloride (10 Gm. four times a day) and fluids. Complete recovery follows in from one to four weeks.

MOORE, Boston.

A NOTE ON ARTIFICIAL PYREXIA IN EPILEPSY. F. L. MCLAUGHLIN, Brit. M. J. **2**:724 (Oct. 19) 1935.

Eight adult patients with epilepsy, varying in age from 18 to 58 years, were treated for twenty days with daily intramuscular injections of sulfur in oil. All were subject to frequent major seizures. Some degree of mental deterioration, as well as typical epileptic habitude, was present. During the period of pyrexia the number of attacks in each patient was definitely reduced from that recorded in the preceding twenty days. The mental condition, except in one patient, was favorably influenced during treatment. Improvement, however, proved to be temporary in all the patients treated.

BECK, Buffalo.

AMBULATORY AUTOMATISM IN EPILEPSY. L. MARCHAND, Ann. méd.-psychol. **91**:609 (Dec., pt. 2) 1933.

The term automatic acts of epilepsy describes all the psychomotor manifestations, coordinated or not, produced without the intervention of the will, not requiring higher cerebral functions and usually leaving no recollection. The patient goes about aimlessly and often carries out acts fraught with great danger but emerges unharmed. The patients are not usually seen in a hospital because of the intermittent character of the manifestation. There are three types of ambulatory automatism associated with epilepsy: (1) that shown by persons with the classic type of epilepsy, (2) that exhibited before the onset of convulsive accidents and (3) that which in itself constitutes an epileptic manifestation. The condition is of medicolegal importance, since during these states crimes are often committed and the responsibility must be established.

MOORE, Boston.

CONTRIBUTIONS TO THE STUDY OF THE NARCOLEPSY OF GÉLINEAU. E. WENDEROWIČ, Monatschr. f. Psychiat. u. Neurol. **87**:276 (Dec.) 1933.

The term narcolepsy should be used exclusively to designate the syndrome described by Gélineau. Various hypnoid states observed in neurosis, in certain organic diseases, such as arteriosclerosis and tumor of the brain, and in some metabolic disorders should not be classified under this term. Hypnoid conditions may be divided into three groups: (1) narcolepsia symptomatica, (2) narcolepsia idiopathica and (3) somnus and somniculositas. The last-mentioned group includes states of sleep or drowsiness which may be encountered in neurosis or organic diseases but which do not conform to the clinical picture of Gélineau's disease. The narcoleptic syndrome presents four cardinal features: (1) attacks of sleep during the day, often accompanied by vivid dreams and occurring, in a minority of cases, in a setting of constant drowsiness; (2) vivid dreams at night, with restlessness and talking or screaming during sleep; (3) sudden attacks of loss of muscular tone, without loss of consciousness, usually brought on by emo-

tional stimuli, and (4) more lasting attacks of flaccidity which are observed in the waking state. They are frequently noted on awakening from sleep or after reclining in the daytime and are often associated with a feeling of marked anxiety. Other less common symptoms are adiposity, a moderate degree of diabetes insipidus, general hyperhidrosis and dryness of the mouth. Relative lymphocytosis has been reported in some cases. Wenderowič believes that narcolepsy is based on organic disease of the diencephalic or mesencephalic apparatus which regulates sleep and the waking state. Endocrine dysfunction is not of primary importance but may play a secondary rôle in the pathogenesis of the syndrome. Studies of epidemic encephalitis have shown that narcolepsy can be caused by exogenous factors. Cases have also been described in which malaria, trauma and post-vaccinial encephalitis were followed by narcolepsy. It is problematic whether or not there is true endogenous narcolepsy based on an inherent or inherited inferiority of certain definite areas of the nervous system. Wenderowič looks on the narcoleptic syndrome as an expression of loss of function and not as a manifestation of an irritative lesion. He believes that the four cardinal features can be attributed to hypofunction of one complex physiologic apparatus, the function of which is to transform muscular and mental processes from the sleeping to the waking state and to hold the organism in the latter condition.

ROTHSCHILD, Foxborough, Mass.

Treatment, Neurosurgery

STREPTOCOCCIC MENINGITIS: REPORT OF TWO CASES WITH RECOVERY. MENDEL ZELIGS, Am. J. Dis. Child. **50**:1497 (Dec.) 1935.

Two cases of verified streptococcic meningitis are described, one in a girl aged 6 years with streptococcic meningitis following trauma to the skull and spontaneous drainage of spinal fluid through the nose as a result of basal fracture of the skull. Treatment in this case consisted of daily lumbar puncture and daily intravenous injections of 10 cc. of antistreptococcus serum. The second case was that of a boy aged 11 years in whose case purulent streptococcic meningitis developed and daily lumbar punctures were made, with removal of fairly large quantities of cerebrospinal fluid. After this, injection of air was performed. This procedure was continued daily for nine days. Zeligs comments that a number of European workers have used gas of various types in the treatment of meningitis.

WAGGONER, Ann Arbor, Mich.

PRACTICAL CONSIDERATIONS RELATING TO FAMILY CARE OF MENTAL PATIENTS. HORATIO M. POLLOCK, Am. J. Psychiat. **92**:559 (Nov.) 1935.

Mentally diseased and defective persons of certain types may be safely cared for in private families. This procedure is advantageous to the community because it is cheaper, to patients with mental disease in institutions because there will be fewer in the hospitals and to the patients themselves because of the advantages of domestic over institutional environment. Three systems of family care are in use, the Belgian, the Scottish and the German. With the Belgian (Gheel) plan, small district offices of the state hospital are scattered throughout the community; in families near each of these offices patients are placed. The office serves as a center both for advice and for recreation for the patient, and as a half-way house between the hospital and the family. With the Scottish system, patients are placed in widely separated and scattered homes. The German system places the patient in his own home, under the care and supervision of a visitor from the hospital. Probably only the Gheel plan would be applicable to the problem in the United States.

The patients suitable for placement in families include those with quiet schizophrenia, those with simple defectiveness and others who have a settled

routine and are not likely to make trouble or need constant medical or custodial supervision. Physically ill, quarrelsome, deteriorated, suicidal or violent patients are not proper subjects for family placement. If possible, only homes in small communities which possess garden plots where vegetables or flowers may be raised should be used. The supervising visitors should come at irregular intervals to examine the progress the patient has made, but too much supervision must be avoided. An occupational therapeutist should also visit the patient at more or less regular intervals to work out a vocational plan. The good will of the public must be enlisted in order to encourage the registration of good rather than of unsuitable families. The maximum rate paid should be somewhere between the usual boarding rate in the community and the average cost of maintaining a patient in an institution. At present, Massachusetts and New York (the only states in the United States in which the system is used) pay a maximum of $4.50 and $4 a week, respectively. A low rate usually means a low standard of care. Even a high rate will mean a great saving to the state, as long as it is under the average cost of institutional maintenance. Some plan for extra-institutional placement of many mentally ill patients must be adopted sooner or later, for the hospital system cannot continue to grow indefinitely to accommodate the increasing numbers of persons who are insane.

DAVIDSON, Newark, N. J.

EXCRETION OF MERCURY AFTER CLINICAL INTRAMUSCULAR AND INTRAVENOUS INJECTIONS. TORALD SOLLMANN, NORA SCHREIBER and H. N. COLE, Arch. Dermat. & Syph. **32**:1 (July) 1935.

Mercury injected into the body is not clinically effective in the treatment for syphilis unless it remains diffusible and dissociable. The extent to which this occurs can be measured by the amount and consistency of the mercurial output in the urine. If by the end of the fourth week of treatment 0.5 mg. or less of mercury is found in the total daily urinary excretion the treatment must be considered ineffective. On the other hand, when the daily output of mercury in the urine exceeds this amount, particularly when it exceeds 0.8 mg., the treatment may be considered as effectively antisyphilitic. Accordingly, methods of mercurial treatment may be divided into the two groups: those yielding less and those yielding more than a daily output of 0.5 mg. of mercury. In the first or ineffective group are included: (1) inunctions with either 5 per cent ointments of metallic mercury and mercury oleate or ointments of mild mercurous chloride; (2) intravenous injections of mercuric oxycyanide; (3) standard intramuscular injections of the benzoate; (4) intravenous injections of mercurosal, and (5) oral administration of 15 mg. of mercuric chloride a day. In the second or effective group are included: (1) oral administration of 0.2 Gm. of mercury with chalk daily; (2) ordinary and massive inunctions; (3) daily intramuscular injections of mercuric sodium bromide, and (4) weekly intramuscular injections of mercuric oil.

DAVIDSON, Newark, N. J.

MAPHARSEN IN THE TREATMENT OF SYPHILIS: A PRELIMINARY REPORT. O. H. FOERSTER, R. L. MCINTOSH, L. M. WIEDER, H. R. FOERSTER and G. A. COOPER, Arch. Dermat. & Syph. **32**:868 (Dec.) 1935.

Mapharsen is a trivalent arsenical. The arsenic content is about the same as that of the arsphenamines, but since the therapeutic dose is smaller the patient receives much less arsenic per therapeutic unit. Initial doses of 25 mg. were well tolerated, although they often produced a mild and transient Herxheimer reaction. Subsequent doses of 60 mg. each were received by most of the patients without toxic effect. Serial examinations of serum expressed from chancres showed that within twenty-four hours after an injection of 60 mg. of mapharsen most of the smears were free from spirochetes. The other visible syphilitic lesions generally healed promptly during a course of therapy. In most cases the reaction of the blood serum was rendered negative by the administration of mapharsen. In 131 patients

receiving 2,117 injections, immediate toxic reactions were noted; however, in all but 30 instances it was of a mild type. In 4 patients jaundice developed. The authors urge a further and longer clinical trial of mapharsen, believing that its potent antisyphilitic possibilities justify more extensive study.

DAVIDSON, Newark, N. J.

THE EFFECTIVE USE OF SMALL NON-DEHYDRATING DOSES OF EPSOM SALT IN EPILEPSY. ALEXANDER WOLF, J. Neurol. & Psychopath. **16**:213 (Jan.) 1936.

Depression of the blood magnesium has been known to produce various convulsive states. Conversely, elevation of the blood magnesium has been applied therapeutically because of its sedative effect. In view of these findings, Wolf administered by mouth small nondehydrating doses of magnesium sulfate (from 0.6 to 17 Gm.) to seventy-four selected patients with epilepsy. Thirty-five patients used as controls were given liquid petrolatum. The average normal value for magnesium per hundred cubic centimeters of whole blood was found to be 3.61 mg., as compared with 3.47 mg. in cases of epilepsy. Fifty-eight per cent of the patients who were treated showed definite improvement, and only 12 per cent of those in the control group were slightly benefited. No correlation was found to exist between the degree of improvement, the quantity of the drug administered and the level of magnesium in the blood. Magnesium may be effective in some patients with epilepsy, but not because of magnesium deficiency or of dehydration.

MALAMUD. Ann Arbor, Mich.

TREATMENT OF DYSMENORRHOEA BY ALCOHOL INJECTION. ALBERT A. DAVIS, Lancet **1**:80 (Jan. 11) 1936.

Injection of alcohol has been employed by Davis in six cases of dysmenorrhea, with complete and apparently permanent relief. In three of these instances cervical dilatation was performed at the same time. It is Davis' opinion that his results indicate the superiority of this operation over ordinary dilatation. He explains the relief of dysmenorrhea which follows the operation by the interruption of sensory and motor pathways and of irregular ovarian influence. Davis considers the danger of perforation of the rectum, with consequent cellular infection and injury to the ureter and uterine artery to be slight.

Injection of alcohol for the relief of dysmenorrhea was first introduced by Blos in 1929. A modification of Blos' method of infiltration was used by Young in the treatment for the syndrome named by him broad ligament neuritis, with excellent results.

WATTS, Washington, D. C.

VENTRICULOGRAPHY BY OPAQUE INJECTION. E. W. TWINING and G. F. ROWBATHAM, Lancet **2**:122 (July 20) 1935.

Twining and Rowbatham describe two cases in which thorium dioxide was used in ventriculography. The first patient was an engine driver, aged 50, who complained of severe generalized headaches, of sudden onset, associated with vomiting, drowsiness and lack of interest in the surroundings. Ten cubic centimeters of air was injected, followed by 10 cc. of thorium dioxide. Roentgenograms were made within fifteen minutes and showed an even density in both ventricles. Roentgenographic examination two hours later showed that almost all the thorium had left the ventricular system.

In a second case ventriculography by injection of thorium dioxide demonstrated an acoustic neuroma on the right side and showed clearly the normal outline of the lateral and third ventricles and the aqueduct of Sylvius.

Twining and Rowbatham found thorium dioxide to be freely miscible with cerebrospinal fluid. They believe that roentgenographically the results surpass those with injection of air in density and definition and in the ease with which the whole ventricular system can be shown, not only in its main features but in

its fine details. Stereoscopic views were extremely satisfactory, It is the opinion of the authors that the method offers the great advantage that intracranial tension is unaltered and that the not inconsiderable risk of replacement with air (estimated by some authors to result in a mortality of 10 per cent) is obviated.

WATTS, Washington, D. C.

THE ROEHMER TREATMENT FOR CHRONIC ENCEPHALITIS. AMOS CHIABOV, Rassegna di studi psichiat. **24**:673 (July-Aug.) 1935.

Chiabov uses the Roehmer method of treating patients with chronic encephalitis, consisting of the administration of a 0.5 per cent solution of atropine sulfate, each drop of which contains about 0.25 mg. of atropine. The treatment consists in the administration on the first day of 1 drop after each principal meal. The dose is increased every day by 1 drop three times a day, so that in the first few days 15 drops of the solution are administered, which corresponds to 3.5 mg. of atropine a day. After this first period treatment is discontinued for about a week and is resumed by gradually increasing the number of drops after each meal to a maximum of 10, thus bringing the total daily intake to 30 drops a day, or 7.5 mg. of atropine. This step represents the most trying period of the treatment, for the patient, not yet favorably influenced by the atropine, suffers from all the symptoms of atropinism. If treatment is continued with this dosage for fourteen days the disturbances due to atropine gradually disappear, and its beneficial effect becomes manifest.

The author then increases the dose from 10 to 15 drops after each meal, i. e., a total of 45 drops a day, or the equivalent of 10.5 mg. of atropine, and again to 60 drops, or 14 mg. of atropine daily.

At this period phenomena of intolerance appear in some cases in the form of short confusional episodes, rapid increase in the pulse rate and rapid loss of weight. In such cases the dose of atropine should be diminished rapidly but not stopped suddenly, in order to avoid phenomena of abstention. In two of the cases in the author's series an old process of tuberculosis became reactivated, and in one death followed the total suspension of atropine medication. For patients without signs of intolerance, Chiabov gradually increases the dose to a maximum of 40 drops three times a day, i. e., 120 drops per day, or the equivalent of 30 mg. of atropine.

The results of the Roehmer treatment seem to be encouraging. The hypertonus and rigidity are particularly influenced, and patients who were not previously able to care for themselves become able to do so.

FERRARO, New York.

Special Senses

DIAGNOSTIC VALUE OF DEFECTS IN THE VISUAL FIELDS AND OTHER OCULAR DISTURBANCES. JOSEPH H. GLOBUS and SIDNEY M. SILVERSTONE, Arch. Ophth. **14**:325 (Sept.) 1935.

Globus and Silverthorne have based their article on 171 verified cases of supratentorial tumor of the brain. The following questions were investigated specifically: (1) the value in localization of tumor of the brain of studies of the visual fields and observations on other ocular disturbances, such as diminished acuity of vision, papilledema, atrophy of the optic nerve, alterations of the pupillary reflex and ocular palsy; (2) the frequency with which the observations at operation or autopsy corroborate the clinical diagnosis, particularly when necropsy is based on defects in the visual fields, and (3) the factors aside from the location of the tumor which are responsible for the presence or absence of the commonly characteristic ocular disturbances.

In tumor of the frontal and prefrontal regions, the syndrome of homolateral atrophy of the optic nerve and contralateral papilledema, i. e., the Kennedy syndrome, was found in only one of forty cases.

The authors' conclusions are as follows:

"It is obvious that the number of tumors reported here in which perimetry was of diagnostic assistance is not large. This is a somewhat discouraging feature, particularly in view of the current belief that careful perimetry and other studies of the eyegrounds will serve as secure leads in the identification of the site and possibly the character of the expanding lesion. However, consideration must be given to the fact that attempts to obtain reliable visual fields were often frustrated by the poor cooperation of the patient or by the advanced diminution of visual acuity caused directly or indirectly by the lesion. Of greater significance, however, is the fact that characteristic defects in the visual fields, when obtained at any period of the clinical course by reliable observers with the full cooperation of the patient, are of immense diagnostic service. It seems reasonable to assume that studies of the visual fields when carried out earlier in the clinical course may yield in a fair number of cases highly useful diagnostic leads for the localization of temporal, temporo-occipital and interpeduncular tumors; and that whenever defects in the visual fields are obtained under satisfactory conditions they are usually substantiated by operation or by the findings at necropsy.

"It is, however, essential to bear in mind that there are several anatomic factors aside from the location of the tumor which frequently cause deviations from the characteristic visual disturbances. By virtue of its infiltrating character a tumor may spare the optic pathways as it invades the intercellular and interfibrous spaces, or it may encroach on the optic pathways in an irregular fashion, and thus cause great variability in the defects of the visual fields. Indirect pressure, particularly when caused by an encapsulated tumor, constitutes another factor which must be considered in an attempt to explain deviations from typical disturbances of the visual mechanism."

SPAETH, Philadelphia.

ANALYSIS OF FIFTY-FIVE CASES OF TOBACCO-ALCOHOL AMBLYOPIA. FRANK D. CARROLL, Arch. Ophth. **14**:421 (Sept.) 1935.

At the eye clinic of the Massachusetts Eye and Ear Infirmary amblyopia due to tobacco and alcohol was seen in from 0.3 to 0.5 per cent of new patients. There is a large number of patients in whom the condition apparently remains undiagnosed and who remain untreated for many months after the diagnosis should have been made. Ninety-eight per cent of the cases occur in males and 2 per cent in females. One case was that of a boy aged 13 who had all the symptoms typical of tobacco amblyopia, and also a tobacco heart. Seventy-six per cent of the patients were over 50 years of age, and in the entire series Italians were more often affected than persons of any other nationality. The disease seemed to occur in all social classes.

Among the outstanding points of interest in a series of 55 patients studied intensively is the relationship of abstinence to improvement. Patients sometimes improved without markedly decreasing the use of tobacco and alcohol. There was great variability in the normal course of the disease. Amblyopia may develop after the use of only moderate quantities of tobacco and alcohol. Traquair noted that in England patients suffering from tobacco amblyopia belong almost entirely to the respectable working class and that the kind of person who can be regarded as a "soaker" is seldom found among them. This was not found to be true in this country.

SPAETH, Philadelphia.

THE REATTACHED RETINA. EDMUND B. SPAETH, Arch. Ophth. **14**:715 (Nov.) 1935.

In this article physiologic, ophthalmoscopic and microscopic observations and comparisons were made in regard to the reattached retina after successful surgical intervention for retinal detachment. It is probable that the retina under such circumstances responds differently to various stimuli. The color sense, in some instances, shows unusual and bizarre disturbances which are not wholly regular. The light sense threshold is definitely raised, whereas the central visual acuity seems to be more nearly normal than the light sense threshold. Spaeth believes

that sensitivity of the peripheral form field and central visual acuity involve gross epicritic responses and that perfection in retinal details is not as essential for ready improvement in form perception after successful surgical intervention, as compared with the demands made on the retina for the determination of a normal light sense threshold after dark adaptation. SPAETH, Philadelphia.

PARACENTRAL HOMONYMOUS HEMIANOPIC SCOTOMA. OTTO BARKAN and S. F. BOYLE, Arch. Ophth. **14**:957 (Dec.) 1935.

Homonymous hemianopic scotoma is a rare condition. Only a small number of cases have been described. Two were reported previously by Barkan and Barkan, and Barkan and Boyle now report a third. The symptom complex consists of difficulty in reading, absence of reduction in central visual acuity, characteristic changes in the fields, namely, a homonymous scotoma which does not include the macula, with maintenance of the peripheral field and an untouched portion of field lying between the periphery and the scotoma, and normal ophthalmoscopic findings.

Barkan and Boyle report a case of paracentral scotoma in a woman aged 60, with high blood pressure and a history of cranial trauma. They believe that the lesion first involved the maculas but later retracted. SPAETH, Philadelphia.

PAPILLEDEMA AND OPTIC NEURITIS. LESLIE PATON, Arch. Ophth. **15**:1 (Jan.) 1936.

The term papilledema was first used in cases in which the nerve head showed more than 2 diopters of swelling, the term papillitis being retained for more moderate degrees of optic neuritis. In 1911 Holmes and Paton first used the term papilledema to describe all forms of edema of the nerve head due to increased intracranial pressure. They distinguished between papilledema with no primary inflammatory changes and papillitis in which the swelling of the disk was associated with inflammatory changes and loss of function. True optic neuritis, as distinguished from papilledema, was then regarded as manifesting itself in two ways: either as retrobulbar neuritis or as papillitis, the only essential difference being in the site of the inflammatory change.

Paton reaffirms his theory of the mechanism of formation of papilledema presented in 1911. This stated that the rise of pressure in the intracranial fluids is transmitted from the cisterna basalis along the sheath of the optic nerve. In order to maintain the circulation in the intravaginal portion of the central vein against this increased pressure in the sheath there is a rise in venous pressure in the central vein and, in consequence, in the whole retinal circulation. This obvious venous engorgement resulted in increased formation of lymph. The main lymph channels draining the disk and posterior part of the retina pass back into the nerve sheath, and the increased pressure in the vaginal sheath blocks also the normal drainage of lymph. Production of the edema and swelling of the disk are due therefore, to these factors: increase in the production of lymph caused by increased venous pressure and block in the drainage of this lymph.

Paton believes that differences in the level of papilledema are of value in indicating the side on which the tumor is located. He calls attention to the assertion of Parker that one of the factors which may cause inequality in the swelling of the disks is inequality in intra-ocular tension and that the eye with the lower intra-ocular tension will show swelling of the disk sooner than the other.

Anatomic structures of the nerve head, not in themselves pathologic, also may modify the amount of papilledema. Paton showed a disk which was swollen to a height of 4.5 diopters on the nasal margin while the temporal margin remained flat. This difference was due to the density of connective tissue, preventing development of swelling on one part of the disk and leaving the physiologic pit clear.

In the second part of the paper Paton discusses the various causes of optic neuritis from a histologic standpoint. In regard to tabetic atrophy of the optic nerve he states: "I wish only to reiterate what I said in 1922 when I concluded from a careful examination of the visual fields and the variability in the type of visual loss that the attack on the nerve might in some cases be interstitial and in other cases parenchymatous."

In speaking of the various obscure viruses which affect the optic nerve, Paton emphasizes the relationship which exists between herpes ophthalmicus and varicella, the one being a dermatotropic and the other a neurotropic manifestation of the same virus. Further, herpes ophthalmicus is one of the virus diseases which rarely attacks the optic nerve on the affected side. Hutchinson described the first case of this disease in 1866. In 1923 Paton described two such instances, one immediately after the other, in both of which blindness resulted. In the one case of acute disseminated encephalitis which came to his attention, the disease followed an attack of chickenpox, and he believes that in most of the cases reported this condition followed varicella, vaccinia or measles. He outlines four important points relating to the optic neuritis associated with these various conditions: (1) Loss of sight precedes the ophthalmoscopic changes; (2) the ophthalmoscopic changes are of brief duration; (3) the disks may show no trace of change after the swelling has subsided, and (4) recovery of vision is usually synchronous with the subsidence of the swelling.

SPAETH, Philadelphia.

THE NERVE SUPPLY TO THE ORBICULARIS MUSCLE AND THE PHYSIOLOGY OF MOVEMENTS OF THE UPPER EYELID. MORRIS B. BENDER, Arch. Ophth. **15**: 21 (Jan.) 1936.

Downward rotation of the eyeball is normally associated with a corresponding movement of the upper eyelid. When an attempt is made to look downward with the eyes closed, the lids open slightly and assume a position normally taken in downward gaze. Defective central or peripheral innervation of the orbicularis palpebrarum, levator palpebrae or Müller's muscles may alter these movements. Bender describes an unusual example of abnormally associated movements of the upper eyelid in a case of osteochondroma. A left frontotemporal craniotomy was performed and a calcified tumor removed; the tumor extended laterally from the sphenoid ridge to the sella turcica. The changes in the ocular muscle were as follows: (1) there were paralysis of the superior and inferior rectus and oblique muscles and slight weakness of the external rectus muscle; (2) the pupil was in middilatation and was fixed to direct and consensual light stimuli, in accommodation and to reflex sympathetic and cocaine stimulation; (3) there was no ptosis, although the left palpebral aperture was slightly smaller than the right; there was slight enophthalmos; the tarsal portion of the superior lid appeared atrophic, and the superior palpebral fold was prominent; (4) the patient was able to close the eyelids at will, with equal force on the two sides. On looking down, however, the left upper eyelid lagged, while the left eyeball turned slightly inward. In attempting to look down with both eyes closed, the left eyelid snapped upward and assumed the same abnormal position as in downward gaze; on looking up the two eyelids were equally retracted, and the left eyeball turned slightly inward. There was no change in the size of the palpebral opening in looking to the right or to the left, nor was there any difference after the local application of cocaine to the left eye. The diameter of the pupil was not altered during any of the ocular movements. Direct and consensual corneal reflexes were elicited bilaterally even when the left upper lid remained elevated during the act of looking down. Blinking movements in the left eye, which under normal conditions should be synchronous with those in the right, were frequently omitted. The latter abnormality was evident so long as the eyes remained open, the position of the globes having no effect on the deficiency of the blinking movements in the left eye. The right eyelid showed the normal associated position and movement.

The various types of abnormally associated movements of the lid are:

Series I.—Cases in which certain movements of the lower jaw are associated with an upward movement of the eyelid.

Group 1: Cases of unilateral congenital ptosis in which the drooping eyelid is raised both when the mouth is opened (digastric muscle) and when the jaw is directed to the opposite side (external pterygoid muscle).

Group 2: Cases of unilateral congenital ptosis in which the drooping eyelid is raised when the jaw is depressed but is not raised with lateral movements of the jaw.

Group 3: Cases of unilateral congenital ptosis in which the drooping eyelid is raised with lateral movements of the jaw (external pterygoid action) but not with the simple opening of the mouth (Marcus Gunn phenomenon).

Group 4: Cases in which similar associated movements of one upper eyelid occur with movements of the lower jaw, but in which there is no ptosis.

Series II.—Cases in which contraction of the levator palpebrae superioris muscle is associated with contraction of the rectus internus muscle.

Series III.—Cases of paralysis or paresis of one external rectus muscle in which movement inward of the affected eye is associated with contraction of the orbicularis muscle and retraction of the globe. All such cases occur in children under 9 years and date from infancy.

SPAETH, Philadelphia.

THE PUPILLARY REACTIONS IN COMBINED LESIONS OF THE POSTERIOR COMMISSURE AND OF THE PUPILLODILATOR TRACTS. N. P. SCALA and ERNEST A. SPIEGEL, Arch. Ophth. **15**:195 (Feb.) 1936.

This paper is a contribution on the pathogenesis of the Argyll Robertson pupil. The experiments were performed on cats. It was found that unilateral severance of the posterior commissure produces slight homolateral mydriasis and diminution but not loss of the light reflex. If this lesion is combined with section of the central pupillodilator pathways, slight miosis of the homolateral pupil results, and the dilator response of the corresponding pupil to painful or emotional stimuli is diminished but not abolished. After the instillation of atropine into both eyes the miotic pupil dilates somewhat more slowly but reaches finally nearly the same extent of dilatation as that of the opposite pupil. Such combined lesions do not produce the picture of the Argyll Robertson pupil in cats. Scala and Spiegel believe that the assumption of a lesion of the synapse between the afferent and the efferent part of the pupillary light reflex arc gives the best explanation of all the symptoms of the Argyll Robertson pupil.

SPAETH, Philadelphia.

PAGET'S DISEASE AND DEAFNESS. J. R. LINDSAY and H. B. PERLMAN, Arch. Otolaryng. **23**:580 (May) 1936.

In four of twenty-five cases of Paget's disease at the University of Chicago definite impairment of hearing was presented. These cases are reported in detail. The diagnosis was corroborated by roentgenography, and in two cases, by biopsy. The hearing tests indicated otosclerosis. Other evidences of Paget's disease were present. There were pink color of the promontory, increased bone conduction and marked loss of hearing for high notes. The findings in two cases suggested changes in the foot-plate of the stapes. Osteitis deformans may produce conduction deafness or nerve deafness, although it is possible that otosclerosis may accompany osteitis deformans. It is believed that a careful study will rule out otosclerosis.

HUNTER, Philadelphia.

THE RESPONSES OF CATERPILLARS TO SOUNDS. DWIGHT ELMER MINNICH, J. Exper. Zoöl. **72**:439 (Feb.) 1936.

Seven species of butterfly larvae and eight species of moth larvae, belonging to seven families, were found to be responsive to sounds produced by tuning-

forks. The response consisted of instant cessation of movement or contraction of some of the longitudinal muscles or both types of reaction. There was species variation in the form and intensity of the response. Previous mechanical stimulation temporarily reduced or inhibited the response to sound. The experiments showed that the receptors involved are not confined to the head, the thoracic legs or the anterior third of the body. They are certainly present in the middle third of the body and apparently in the anterior third also. The responses were essentially the same in relatively hairless and in very hairy species, thus raising the question whether structures other than hairs may not be involved in the responses to sound. The results, together with those previously reported by other investigators, suggest that the response to sound is characteristic of many, perhaps of all, caterpillars.

WYMAN, Boston.

ATROPHY OF THE OPTIC NERVE AND MALARIA THERAPY. C. WESKAMP, Ann. d'ocul. **172**:449 (June) 1935.

The optic nerve may react to syphilitic infection in two ways: (1) the inflammatory form, with the histologic characteristics of syphilitic lesions, and (2) the atrophic form, with lesions of diffuse sclerosis without syphilitic characteristics. These conditions result in two characteristic syndromes, which differ ophthalmoscopically in their evolution, treatment, prognosis and pathogenesis. The syphilitic etiology is the only factor common to the two syndromes.

In the inflammatory form the parasite or its toxins, working in situ, determine the neural reaction, which is manifested by neuritis or by a gumma of the optic nerve. Antisyphilitic treatment is usually efficacious, and the prognosis depends on early treatment. In the atrophic form the optic disk is white and sharply defined, and the arteries are contracted but not inflamed. Antisyphilitic treatment is ineffective, whether mercury, arsenic or bismuth is used and whether administration is intramuscular, intravenous, intraspinal or intracisternal.

In 1866 von Graefe stated: "The forms of syphilitic optic atrophy have a fatal prognosis. They constitute a *noli me tangere* for the experienced and wise physician, for it is difficult to improve and easy to aggravate the disease."

Pathogenesis is also uncertain. Does the syphilitic virus or its toxin act directly either on the ganglion cells of the retina or on the optic fibers, or do these elements, as Abadie stated, atrophy as the result of vascular spasm caused by a distant lesion localized in the medulla? These questions are still unsolved.

During the past few years malaria therapy for dementia paralytica has stimulated fever therapy for simple atrophy of the optic nerve. Weskamp reports his experience with malaria therapy in sixteen cases of simple atrophy of the optic nerve as follows: Improvement was observed in eight cases; in five the patient showed a slight degree of improvement, and the result in one case was doubtful and in two cases was reported as a failure.

Since statistics have proved that the atrophic process rarely continues longer than three years, only cases in which observation was made for three years after treatment are reported. This treatment was successfully applied in atrophy of different degrees. The results obtained lasted for more than three years; in case 1, for example, improvement was maintained for seven years.

After the malaria treatment, arsenic, bismuth and mercury were administered. If the visual field began to contract atropine was injected.

BERENS, New York.

PAPILLORETINITIS OF DENTAL ORIGIN. P. BONNET and BUSSY, Ann. d'ocul. **172**: 494 (June) 1935.

Bonnet and Bussy report a case of papilloretinitis of dental origin in which papilledema disappeared completely and slight postneuritic atrophy resulted. The many exudates which covered the retina were almost reabsorbed. The macula presented a fissured, grayish aspect; consequently, visual acuity did not exceed ⅓.

BERENS, New York.

A New Theory of the Pathogenesis of the Argyll Robertson Sign: Relation to Pupillary Movements. A. B. Uriarte, Ann. d'ocul. **172**:672 (Aug.) 1935.

The clinical picture known as the Argyll Robertson sign is a syndrome composed of: (1) loss of the light reflex; (2) miosis (in a number of cases); (3) loss of sensory, sensorial and psychic movements; (4) preservation of the accommodation-convergence reflex; (5) preservation of the Pilz-Westphal reflex; (6) changes in the stroma of the iris, and, frequently, (7) inequality and irregularity of the pupils. The first clinical evidence of the Argyll Robertson sign is paralysis of the dilator muscle of the iris. In a case of miosis, with pupillary irregularity, loss of the sensory, sensorial and psychic reflexes and atrophy of the stroma of the iris, it seems natural to Uriarte to suspect paralysis of the dilator muscle.

It is difficult to suppose that the dilator muscle is never paralyzed. It is also surprising that in ophthalmology a syndrome of paralysis of the dilator muscle is not described. In reality, the Claude Bernard-Horner syndrome is not complete paralysis of the dilator muscle, for this muscle retains all its action. In a case in which the Argyll Robertson sign is incomplete and the light reflex is diminished (pupillary weakness), the sensory, sensorial and psychic pupillary reactions are in agreement with the diminution of the light reflex.

If a luminous ray is projected on the retina of an eye showing diminution of the light reflex (pupillary weakness) in association with pupillary irregularity, the weak pupil reacts slightly. It is of interest that the least contracted sector of the pupil makes the greatest movement. This least contracted region of the pupillary border must correspond to the least altered and consequently the most mobile part of the dilator muscle.

If a strong ray of light is projected on the pupil of a normal eye the pupil contracts to a certain diameter which it does not surpass, no matter how intense the luminous source may be. If, in spite of this extreme contraction to light, the eye is permitted to make an effort of convergence and accommodation the pupil contracts further. Therefore, according to Uriarte's new interpretation, the light reflex (dilatation) and accommodation (contraction) are independent movements; i. e., they have their own pathways and a different physiologic action.

Uriarte concludes: (1) The classic theory of pupillary reaction to light, as well as the universally accepted course of the reflex arc, is not justified physiologically; (2) the classic interpretation of the pupillary light reflex does not explain the pathologic behavior of the pupil; (3) if it is believed that the light reflex is a movement of dilation the pathologic action of the pupil is made clear, and (4) the phylogenetic development of the movements of the diaphragm of the iris is in accord with Uriarte's interpretation and not with the classic physiologic theory.

Berens, New York.

Comparison of the General Blood Pressure with the Pressure in the Retinal Vessels: Relation of Intra-Ocular Tension to Atrophy of the Optic Nerve. M. Lauber, Ann. d'oçul. **172**:706 (Aug.) 1935.

According to Lauber, the pathogenesis of atrophy of the optic nerve is explained by a disproportion between the blood pressure and the intra-ocular tension. The general hypotension associated with normal intra-ocular tension leads to atrophy; the same is true for normal general tension associated with intra-ocular hypertension (glaucoma). Therapy should consist in raising the general pressure in general hypotonia and lowering intra-ocular tension. Some methods of administering antisyphilitic treatment often induce hypotonia. Examination of the general blood pressure and the general condition is indispensable in the course of syphilitic treatment in order to avoid the development of atrophy of the optic nerve.

Berens, New York.

THE SYNDROME OF THE FLOOR OF THE ORBIT. C. DEJEAN, Ann. d'ocul. **172**:707 (Aug.) 1935.

Dejean states that the syndrome observed in two patients, aged 44 and 56 years, respectively, evolved in three successive phases: (1) the onset, which is characterized by signs of compression of the superior maxillary nerve, violent orbitofacial neuralgia and more or less complete anesthesia; (2) a static phase, in which the orbit is attacked by a new growth and there are severe pains with anesthesia in the region of the first two branches of the trigeminal nerve, diplopia caused by lesion of nerves or orbital muscles, exophthalmos and metastasis to the cervical ganglia on the same side, and (3) a phase of extension to the apex of the orbit and the middle cranial fossa, in which there are pain continuing in the entire distribution of the trigeminal nerve, with intolerable exacerbations radiating toward the neck, paralysis of the various muscles of the eyeball, exophthalmos, anorexia, dysphagia and terminal cachexia.

BERENS, New York.

TRAUMATIC BILATERAL PARALYSIS OF THE SIXTH NERVE. P. DUPUY-DUTEMPS, Ann. d'ocul. **172**:707 (Aug.) 1935.

Dupuy-Dutemps reports a case of cranial traumatism followed by coma, hemorrhage from the ear, paralysis of the sixth nerve bilaterally and paresis of the right side of the face. Functional disturbances disappeared within a few months. The hypothesis of compression or, more probably, of contusion of both nerves is considered.

BERENS, New York.

SEVERAL CASES OF OCULAR NYSTAGMUS, SPONTANEOUS OR INDUCED. H. TILLÉ and G. FRUCHON, Ann. d'ocul. **172**:707 (Aug.) 1935.

From a study of ten cases of ocular nystagmus Tillé and Fruchon emphasize the following features of ocular nystagmus: (1) congenital character; (2) special character, whether pendular or rotatory, vertical or irregular or increasing or decreasing under certain conditions (occlusion, fixation, upward gaze, convergence and light or darkness); (3) common association with strabismus, correction of which decreases the nystagmus; (4) decrease in visual acuity of the fixing eye when the other eye is covered in cases in which nystagmus increases and improvement in vision when one eye is occluded in cases in which nystagmus diminishes; (5) normal reactions to vestibular tests, and (6) frequent but not constant mental deficiency of subjects of the disease (some patients were of superior normal intelligence).

BERENS, New York.

BLINDNESS WITH PAPILLEDEMA AND CENTRAL SCOTOMA AND ENDONASAL INTERVENTION. J. RAMADIER, H. GUILLON and MORANCÉ, Rev. d'oto-neuro-opht. **13**:256 (April) 1935.

Ramadier and his associates add their observations in two more new cases to a previous report. In the case previously described restoration of vision to 10/10 was obtained after the opening of closed empyema of the ethmoid cells. The two new cases differed from the first in that no evidence of infection of the sinuses was discovered; nevertheless, immediate amelioration was obtained by endonasal surgical treatment. In the first new case there were papillitis, central scotoma for colors, retraction of the visual field and periorbital pain. Visual acuity was reduced to 1/10. The second patient, when first seen, had optic neuritis and periorbital pain on the right side, and visual acuity was absent. Permission for endonasal operation was refused. Six months later the patient returned with the same syndrome on the left side: pain, rapid reduction of vision to 1/10, papilledema and central scotoma. There was no clinical evidence of infection of the nasal sinuses. The septum was resected, and the posterior ethmoid labyrinth was explored. Vision promptly returned to 7/10, and the pain and central scotoma disappeared. The much discussed question whether to operate in cases of optic

neuritis in which no evidence of sinus infection is shown is still unsettled. The authors advise operation after a certain interval, if treatment has not resulted in improvement.

DENNIS, San Diego, Calif.

EXAMINATION OF VESTIBULAR RESPONSES OF ELEVEN PERSONS WITH STRABISMUS AND OF TWO WITH UNILATERAL MYOPIA, WITH NORMAL OR SUBNORMAL RESPONSES. E. AUBARET, G. E. JAYLE and APPAIX, Rev. d'oto-neuro-opht. **13**:261 (April) 1935.

Aubaret, Jayle and Appaix conclude that in a considerable percentage of cases of strabismus there exist disturbances in the vestibular responses to instrumental tests. These disturbances indicate vestibular hypo-excitability. Aubaret and Jayle, in a second communication (*Rev. d'oto-neuro-opht.* **13**:285 [April] 1935), called attention to the asymmetry of the nystagmus in the two eyes provoked by the turning test in cases of strabismus. The asymmetry appears only when the quick component is toward the direction of action of the muscle producing the strabismus.

DENNIS, San Diego, Calif.

PHENOMENON OF THE "DEAD CHEEK" ACCOMPANYING THE VERTIGO OF MÉNIÈRE. F. J. COLLET, Rev. d'oto-neuro-opht. **13**:665 (Nov.) 1935.

This condition is described as a sensation of numbness of the ear and corresponding cheek ("dead feeling") which accompanies intense vertigo. The histories of four patients, all near 50 years of age, are given in detail. Collet suggests that the most plausible explanation of the mechanism of this phenomenon is angiospasm of the vestibular centers or pathways, which extends into neighboring territory, the nuclei of origin of the trigeminus nerve. Paralysis of the facial nerve accompanying Ménière's vertigo is susceptible of the same interpretation.

DENNIS, San Diego, Calif.

OBJECT OF AND SIGNIFICANCE OF EXPERIMENTAL EXAMINATION OF THE VESTIBULAR APPARATUS IN OPHTHALMOLOGY. E. AUBARET and G. E. JAYLE, Rev. d'oto-neuro-opht. **13**:672 (Nov.) 1935.

While there still exists difference of opinion on the interpretation of tests to differentiate central from peripheral lesions of the vestibular apparatus, the differentiation in general may be made on the basis of the two following characteristics: 1. Labyrinthine disturbances present from their beginning a complete picture, always combining spontaneous nystagmus, reactionary movements and vertigo. On the other hand, central vestibular disturbances are often manifested by a single symptom: marked spontaneous nystagmus without vertigo or falling or falling without spontaneous nystagmus. 2. In labyrinthine disturbances the symptoms are in agreement (falling and reactionary movements are in a direction opposite to that of nystagmus), while in disturbances of central origin there is discordance among the symptoms (falling and nystagmus occur in the same direction, and vertical nystagmus or conjugate deviation of the eyes is present).

Examination of the vestibular apparatus is of interest in the vast domain of otoneuro-ophthalmology and likewise in the purely ophthalmologic field, both from the physiologic and the clinical point of view. The pathologic variations in the ocular statics, which form the basis of strabismus or certain types of congenital nystagmus, are the expression of disturbance not of a single ocular function but, on the contrary, of one of the factors of ocular statics. In certain cases strabismus is due to a disturbance of the static vestibular function. Ocular motility is integrated to a large degree in the labyrinthine system. In a large percentage of cases strabismus exhibits vestibular hypo-excitability; asymmetrical nystagmus due to diminution in the amplitude of deviation of the eye is occasionally observed. In cases of peripheral ocular paralysis asymmetrical or monocular nystagmus is observed when the quick component of the nystagmus is in the direction of action of the paralyzed muscle. If vestibular examinations are practiced systematically in all cases of ocular paralysis it is possible to determine objectively whether

an oblique muscle is involved, since these muscles are actively concerned in the production of rotatory nystagmus. A study of two cases of ocular paralysis in which ocular function had been recovered revealed that at the time of reparation of the oculomotor paralysis the voluntary function was restored while the oculovestibular function was not. This explains essential monocular nystagmus in certain patients in whom mobility seemed normal in each eye.

The following vestibular responses may be observed in the course of paralysis of function of the ocular globes: (1) disappearance of both voluntary and reflex motility; (2) preservation of reflex motility and loss of voluntary movements; (3) preservation of voluntary motility and loss of reflex motility, and (4) loss of provoked rotatory nystagmus, either existing alone or in company with the disturbances just noted. It is probable that certain combinations of disturbances in labyrinthine responses will be found to result from a definite focal lesion. It appears certain that congenital latent nystagmus or nystagmus resulting from exclusion of vision in one eye is not caused by a vestibular disturbance. It is true, however, that latent and vestibular nystagmus may annul or augment their reciprocal effects, depending on whether the direction of the nystagmus coincides or is opposed. This fact proves that tonic impulses of visual origin are present at the level of the ocular musculature. Disturbances in ocular tonus are revealed by the deviations that appear in an amblyopic eye from loss of the tonus of fusion or fixation. These facts have a pathogenic interest in the explanation of strabismus. Strabismus not due to an anatomic lesion may be considered to be caused by a disturbance of one of the several forms of ocular tonus, arising from involvement of the centers or pathways.

DENNIS, San Diego, Calif.

TRANSITORY AMAUROSIS IN THE COURSE OF OBSCURE ENCEPHALITIS. I. ALFANDARY, Rev. d'oto-neuro-opht. **14**:20 (Jan.) 1936.

Alfandary reports two cases of encephalitis, accompanied by headache and rapid loss of vision due to bilateral papillary stasis, with central scotoma in one instance. In both cases the disease ran a course of about seven weeks and ended in complete recovery. The encephalitis was so mild that the amaurosis dominated the clinical picture. It is assumed that the cause of the encephalitis was infection with an unknown neurotropic virus. Alfandary compares these cases with a number of others reported in the literature, in some of which there was endonasal or intracranial surgical intervention. The patients were much improved or cured, irrespective of the type of operation, and the question arises whether they would not have been just as readily cured without operation. Operation is indicated in cases in which the signs of retrobulbar neuritis are associated with papilledema and central scotoma. In one of Alfandary's cases, however, there was an absolute central scotoma. Alfandary believes that frequent ophthalmic examination should be made and, if improvement does not appear or the process is not arrested, surgical measures may be adopted. His conclusions are: (1) In certain cases of encephalitis bilateral optic atrophy and rapidly developing amaurosis are the principal symptoms; (2) the signs of encephalitis may be so discrete as to be overlooked, especially as they ordinarily disappear when vision fails; (3) it is necessary to be prudent in attributing the cure to operation; (4) operation may be useful, but the indications, choice and mode of action are not precise, and (5) in general operation is indicated when medical treatment is inefficacious. The operation of choice is said to be decompression in cases of bilateral optic neuritis and opening of the nasal accessory sinuses when the neuritis is unilateral, but the question is not yet resolved.

DENNIS, San Diego, Calif.

RELATIONS BETWEEN THE VISUAL CORTEX AND THE PRIMARY OPTIC CENTERS AS DEMONSTRATED BY EXPERIMENTAL STUDIES ON MONKEYS. S. PENARD, Schweiz. Arch. f. Neurol. u. Psychiat. **36**:131, 1935.

Penard reports the results of studies of stained frontal sections of the brains of two monkeys (Macacus rhesus) on which Minkowski had previously operated. The dorsal half of the visual cortex with the underlying optic radiation on the left

had been removed in the first animal, and the greater part of the ventral half of the same structures had been removed in the second animal. On the basis of the degenerative changes observed, Penard concludes that the axons of all ganglion cells lying in the external geniculate body terminate in the area striata and, further, that there is a distinct anatomic projection in that the dorsal portion of the geniculate body is connected with the cortex of the occipital operculum (homologous to the occipital pole and posterior portion of the calcarine fissure in man) and the ventral portion with the lips of the calcarine fissure. Fibers from the ventromedial part of the external geniculate body terminate in the dorsal lip of the fissure, and fibers from the ventrolateral part, in the ventral lip. Since the quadrantic hemianopia demonstrated in the monkeys after operation proved to be transitory, a physiologic projection corresponding to the anatomic projection existed only so far as optimal functional relations were concerned. The occipital lobe is connected, chiefly through corticofugal fibers, with the superior colliculus, but the majority of these fibers proceed from the parieto-occipital area (precuneus and cuneus in man), those from the striate area being in the minority. Axons from the pulvinar terminate in both these areas, but it is as yet an open question whether the pulvinar is to be regarded as a primary optic center.

DANIELS, Denver.

HEMIANOPIC HALLUCINATIONS. G. ENGERTH, H. HOFF and O. PÖTZL, Ztschr. f. d. ges. Neurol. u. Psychiat. **152**:399 (March) 1935.

1. *Diagonal Hemianopic Hallucinations.*—Engerth, Hoff and Pötzl report a case of migraine in a man aged 52, who for six days had a transitory upper left quadrantic defect and hallucinatory experiences. For the first two days he had flamelike hallucinations in the left field. He then began to see strange faces resembling theater masks and, finally, colored twigs. All these hallucinatory experiences were noted in the left field, usually moving from above downward and inward. The hallucinatory experiences disappeared as they reached the midline of the visual field. The direction of movement of the images seemed to be parallel to the meridian of the persistent color scotoma, indicating a reversible lesion in the area striata. The authors also note the discontinuous nature of the perceptions due to this lesion in the occipital cortex, as compared with the usual continuum of normal space perception. Electrical stimulation of the cortex of the area striata also causes such discontinuous photopsia. The to and fro movement of images, which at first are unformed, is probably an elementary property of perception due to cortical activity. This is perhaps similar to the waxing and waning of the local sign in space perception.

These hallucinations did not disappear when fixated. Such disappearance of hallucinatory experiences with fixation is probably due to the function of the opposite and intact area striata. In this case, because of the peculiar position of the images in the visual fields and their incurvation, binocular gaze did not fixate these images. These subjective experiences were probably due to vasospasm in one of the smaller branches of the calcarine vessels which run perpendicular to the main branch. In the transmutation of one form of image to another various factors play a rôle, such as the tendency for every one to see symmetrical and geometric figures in unformed visual impressions, the influence of the experiences of the day and the phenomenon of optic allesthesia, especially in accounting for the colored twigs.

2. *Nocturnal and Diurnal Forms of Hemianopic Illusions.*—The second case reported is that of a man aged 52, with a definite history of syphilis, who was admitted to the hospital with left hemianopia and ataxia in the left upper limb. The hemianopia disappeared in four weeks. During this period of regression of the field defect optical illusions were noted.

One or two days after the onset the patient noted strange faces just before falling asleep instead of the real objects toward which he was looking. They occasionally moved from left to right. During the day he saw numbers and lines and sometimes symmetrical figures on the left side of the field of vision, especially

on walls. If he looked at these images, they disappeared. At times they were colored. At other times he noted sparks and flashes of light in the extreme left side of the field of vision. Once he noted a to and fro motion of a spot on a box. In this case the authors note the influence of experiences of the occupation of the day on the pattern of the image. The illusion during the day is similar to that described by Pick after operation for cataract. That part of the brain which is defective in cases of word blindness probably participated in the elaboration of these diurnal experiences. This was therefore a disorder of symbolic function. A tendency to perceive symmetrical and geometric configurations in elementary scotomas was also observed in this case. The color aspect of these illusions depends to a certain extent on disordered function of the area striata, as well as on the influence, perhaps, of vocational attitudes. The rôle of the dream mechanism in the psychologic elaboration of these elementary visual experiences is noted. The area striata probably functions in fusing discontinuous moving images into an optical continuum, which is perceived as a resting object.

SAVITSKY, New York.

Diagnostic Methods

VENTRICULOGRAPHY WITH COLLOIDAL THORIUM DIOXIDE. WALTER FREEMAN, HERBERT H. SCHOENFELD and CLAUDE MOORE, J. A. M. A. **106**:96 (Jan. 11) 1936.

Freeman, Schoenfeld and Moore believe that colloidal thorium dioxide is of great value as a contrast medium for use in ventriculography. It is freely miscible with the ventricular fluid, is of high specific gravity, finding its way into the recesses of the ventricular system, and, on account of its high opacity to roentgen rays, needs to be used in relatively small amounts. In normal patients it is eliminated within four hours and is so inert that it provokes only a mild inflammatory reaction. It preserves the supporting fluid cushion of the brain and avoids the serious constitutional effects of ventriculography with the use of air. The authors used colloidal thorium dioxide for ventriculography in twenty cases, with two deaths. In one case death occurred within an hour or two, and at necropsy a huge infiltrating glioma was observed in the basal ganglia, occluding the foramen of Monro and limiting the injected material to the side of operation. In two cases there was moderately severe reaction, with fever, stiffness of the neck and vomiting, but the symptoms disappeared within a few days. Both these patients had ventricular obstruction. In one case in which tumor of the cauda equina was suspected and the material was injected into the lumbar sac, there was considerable headache, but the patient was already septic due to infection of the urinary tract, so that the febrile reaction could not be estimated precisely. Most of the patients in this series felt transitory discomfort, sometimes amounting to easily controllable headache, although some (without gross lesions) were out of bed on the third day and went home on the fourth. The chief complaint of one patient on the day after operation was that he was not allowed a full diet. He sat up and read in entire comfort except for soreness over the scalp.

EDITOR'S ABSTRACT.

CONTRALATERAL TONODYNAMIC REFLEXES OF THE INTEROSSEAL AND HYPOTHENAR MUSCLES. PAILHAS, Encéphale **30**:509, 1935.

Tonodynamic reflexes have been defined by Laignel-Lavastine, Chevallier and Vié as the automatic execution of a movement by a given group of muscles after an intense and prolonged voluntary effort by that group of muscles. Pailhas observed symmetrical tonodynamic reflexes in the group of muscles contralateral to that which exerts the effort. Such contralateral reflexes can be obtained by executing forced abduction and adduction of the fingers or, abduction of the little finger of one hand while the other hand is relaxed.

LIBER, New York.

Basal Ganglia

LENTICULAR SYNDROME FOLLOWING NITROUS OXIDE NARCOSIS. CYRIL B. COURVILLE, Bull. Los Angeles Neurol. Soc. **1**:30 (March) 1936.

Courville reports the case of a Negress who at the age of 19 years received nitrous oxide anesthesia for an abdominal operation. She failed to regain consciousness for several days, during which time she had three generalized convulsions. She could not speak intelligibly for one month and was completely blind for three months. Thereafter, there developed rigidity and uncontrollable movements. Examination at the age of 27 revealed a childish mental state, involuntary laughter, pallor of the optic disks and generalized rigidity of the extremities, the legs being in flexion. There was atrophy of the small muscles of the hands. The deep reflexes were exaggerated, and the toes were in constant dorsiflexion. Three years later there were definite athetoid movements, and the rigidity was worse. The patient also had syphilitic aortitis.

MACKAY, Chicago.

FIBRILLARY CHOREA OF MORVAN, INFANTILE ACRODYNIA AND PSYCHIC DISTURBANCES. HENRI ROGER and JOSEPH ALLIEZ, Ann. méd.-psychol. **94**:689 (May, pt. 1) 1936.

In 1890 Morvan described under the name *chorée fibrillaire* a peculiar disease; he had seen several cases. The condition is rare, since Roger and Alliez collected only twelve instances, including four of their own, all reported by French authors. The disease is characterized by fibrillary muscular contractions involving the entire body, paroxysms of profuse sweating, erythema and desquamation of the extremities, severe diffuse pains of contusive type, asthenia, tachycardia, increased blood pressure and psychic disturbances consisting of changes of personality, insomnia, anxiety, irritability and extreme agitation, associated in some instances with acute delirium and hallucinations. Roger and Alliez compare the symptoms of Morvan's fibrillary chorea with those of acrodynia and point out the nearly complete similarity of the somatic and, especially, the psychic symptoms in the two conditions. With the exception of fibrillary muscular contractions, usually absent in acrodynia, the essential symptoms are the same—pain in the extremities, desquamation and scalded appearance of the hands, sweating, tachycardia, high blood pressure and psychic disturbances, characterized mainly by changes of personality, depression, irritability, anxiety state and agitation. The mental disturbances in acrodynia are colored by features which are peculiar to the early age of the patients, who are usually children. Thus, the impairment of intelligence and arrest of mental development are likely to be more prominent in association with acrodynia, whereas in Morvan's chorea the intellectual faculties usually remain preserved. The authors suggest that the two conditions belong to the same group of neurotropic virus diseases and possibly are caused by an identical virus. The prominence of psychic-emotional and neurovegetative (sympathetic) disturbances points to a diencephalic localization of the disease process.

YAKOVLEV, Waltham, Mass.

CASE OF POSTTRAUMATIC PARKINSONISM. CONREUR, J. belge de neurol. et de psychiat. **35**:663 (Nov.) 1935.

Conreur reports the case of a patient aged 33 who had always been in good health and had had no infection. While intoxicated he was attacked and badly beaten about the head and face. After this he was incapacitated for a month. About eight or nine months later he noticed tremor of the head and of the upper and then of the lower extremities. For about two years the patient had daily oculogyric crises. There then developed depression, with suicidal tendencies. There were characteristic parkinsonian features. The condition was treated, with some benefit, with atropine sulfate in large doses. Conreur discusses the possibility that this patient's symptoms may have been the result of multiple small hemorrhages in the basal nuclei. He calls attention to several factors which must exist before

the trauma can be blamed for the parkinsonism: The trauma must be sufficiently violent and must occur under conditions in which a cerebral disturbance may be produced; further, an interval sufficient for the development of parkinsonism must follow the trauma, and there must be an uninterrupted progression of symptoms. Conreur concludes that the parkinsonian syndrome may be the result of cranial trauma and that trauma as well as infection must be considered in the etiology of an extrapyramidal syndrome.

WAGGONER, Ann Arbor, Mich.

Experimental Pathology

EXPERIMENTAL AND CLINICAL CATATONIA DUE TO THE COLON BACILLUS. H. BARUK, Ann. méd.-psychol. **91**:449 (Nov., pt. 2) 1933.

Experimental studies were made on cats, guinea-pigs, pigs, pigeons and amphibia, utilizing a culture of Bacillus coli. The organism was obtained from the urine of a patient who had postpuerperal pyelonephritis. Baruk endeavored to show the effect of the neurotropic toxin elaborated by this organism, which is active in the production of catatonia. The toxin was virulent when fresh, but the culture rapidly became attenuated. The general characteristics of the condition produced in animals were catalepsy, flexion, negativism and disturbance of the vegetative functions. There were negativism of the active rather than of the passive type seen in catatonia produced with bulbocapnine and also emotive and impulsive reactions. Polypnea was observed, and the animals were not paralyzed. A longer time was required for the production of catatonia with this toxin than with bulbocapnine. The production of experimental catatonia similar to that seen in dementia praecox adds an argument to the theory of toxic infection as a factor in the genesis of dementia praecox.

MOORE, Boston.

EXPERIMENTAL INVESTIGATIONS ON MULTIPLE SCLEROSIS. IHSAN SCHÜKRÜ, Ztschr. f. d. ges. Neurol. u. Psychiat. **153**:117 (June) 1935.

The frequency of periventricular lesions in cases of multiple sclerosis has impressed many observers with the probability that this disease is caused by a noxious agent present in the spinal fluid. Schükrü injected the spinal fluid of patients with multiple sclerosis suboccipitally into rabbits. Four animals were studied; they died or were killed after three, eight and twelve days and six months, respectively. In the animals which died soon after the injection lymphocytic infiltration was observed in the periventricular regions, with slight increase in glial fibers and early evidence of degeneration of the myelin sheaths. In the rabbit killed after six months definite areas of demyelinization were observed. Serum of patients with dementia praecox was injected suboccipitally into two animals used as controls. No pathologic changes were noted. Schükrü believes that the changes in these animals are identical with the pathologic changes in multiple sclerosis in man.

SAVITSKY, New York.

Society Transactions

LOS ANGELES SOCIETY OF NEUROLOGY AND PSYCHIATRY

Regular Meeting, April 1936

EUGENE ZISKIND, M.D., *President, in the Chair*

ROENTGEN RAYS IN DIAGNOSIS AND LOCALIZATION OF TUMORS OF THE BRAIN. DR. E. B. TOWNE, San Francisco.

There are a considerable number of cases of tumor of the brain, perhaps 20 per cent, in which localization cannot be made without the assistance of roentgen rays. Information to be gained from their application will be considered under three headings: (1) calcification in the tumor, (2) localized thickening or erosion of the skull and (3) cerebral pneumograms.

Calcification in the Tumor—Before the introduction of the Potter-Bucky diaphragm, roentgenographic visualization of calcification in tumors was unknown. In 1923 attention was first called to the fact that some gliomas can be localized by the demonstration of calcification by Dr. R. R. Newell (*S. Clin. North America* **3**:775, 1923) of the Stanford University School of Medicine, who reported 3 cases in which the diagnosis was verified. All were instances of tumor of the frontal lobe and none of the tumors could have been localized by clinical examination. Van Dessel studied Cushing's material and found that in the four and one-half years following the introduction of the Potter-Bucky diaphragm in 1921, a verified glioma of the cerebrum had been demonstrated by roentgenography in 17 of 126 cases (13.5 per cent). In 9 of the 17 cases the tumor was located in the frontal lobe

Localized Changes in the Cranial Bones.—Meningioma (dural endothelioma) frequently causes alterations of the overlying bone, which are demonstrable by roentgen rays. Sosman and Putnam studied the films in 95 cases of verified meningioma in Cushing's clinic and observed "recognizable changes characteristic of the tumor" in 49 per cent. This does not mean that the diagnosis and localization depend on the roentgen findings in any considerable proportion of cases, because in many instances the tumor is easily localized by neurologic examination and in almost all cases there is visible and palpable hypertrophy of the outer table of the skull, which calls attention to the possibility of an underlying meningeal tumor. The roentgenographic demonstration of enostosis has occasionally been of value in localizing a meningioma involving the frontal lobe.

Tumors arising from the eighth nerve in the internal auditory canal have long been known to cause extensive erosion of the petrous bone, but attempts to demonstrate this with lateral roentgenograms have been unsuccessful. I (Erosion of Petrous Bone by Acoustic Nerve Tumor: Demonstration by Roentgen Ray, *Arch. Otolaryng.* **4**:515 [Dec.] 1926) reported 3 cases in which the erosion was clearly shown in posterior projections, which allow comparison of the two petrous bones. Pancoast corroborated these findings. In all cases in which the diagnosis was verified the picture has been positive, but the value is only confirmatory. It is possible that more extensive use of this method for patients complaining of unilateral tinnitus and deafness will allow an earlier diagnosis, which is to be desired in cases of tumor of this region, for the growth frequently reaches a large size before it is identified by clinical findings.

Cerebral Pneumography.—Pneumography, introduced by Dandy in 1918, is by far the most important advance in neurosurgical diagnosis of recent years. All

tumors of the brain produce distortion or change in the size, shape or position of the cerebral ventricles. In pneumography the ventricular fluid is replaced with air through small trephine openings. The roentgen films then give a perfect picture of the ventricular system as a negative shadow, and any abnormalities may, with experience, be detected.

Roentgen rays are thus directly or indirectly responsible for the reduction in the number of cases in which tumor of the brain cannot be localized, from at least 20 per cent to practically zero. This is due partly to improved technic but chiefly to the introduction of the cerebral pneumogram.

DISCUSSION

DR. DORRELL G. DICKERSON: Several years ago Dr. Clement Masson, of New York, published the report of a large series of cases of glioma with calcification. One often sees films of a tumor of the brain with these calcifications. They seem to occur in groups; at least, that has been my observation.

In regard to the Towne sign: Roentgenologists are becoming more proficient in detecting changes around the petrous ridge. Recently I had occasion to send a patient suffering from tumor of the acoustic nerve to a roentgenologist. Without any clinical history he made an exact diagnosis from slight changes at the petrous ridge.

DR. CARL W. RAND. Dr. Towne has shown an unusual number of calcified tumors. Recently I saw the autopsy report in the case of a woman aged 72, who died of carcinoma of the cervix. Since the age of 25 years she had had occasional jacksonian attacks, involving the left side of the face and the left hand. A small calcified, cystic astrocytoma, measuring 3.5 by 5 cm., was observed in the right precentral gyrus, near the arm area. The inference is that the tumor had developed sufficiently to give symptoms of irritation forty-seven years before and that during this period it had increased little in size.

DR. GEORGE H. PATTERSON: There is one type of tumor for which roentgen rays have been of value—a neoplasm of the third ventricle. I have seen 3 instances of a tumor of this region in the last three years. When air is injected into one lateral ventricle of a patient with such a tumor, the third ventricle does not fill and neither does the ventricle on the opposite lateral side. After the air is absorbed, the procedure is reversed; air is injected on the opposite side, and a similar unilateral filling of the ventricle is observed. This is practically diagnostic of tumor of this region.

DR. LEO J. ADELSTEIN: I am greatly interested in Dr. Towne's statement as to the large number of cases of calcification of the neoplasm that he has found in his series of tumors, with particular reference to the gliomas. With the possible exception of cysts of the craniopharyngeal pouch intracranial calcification is most common in cases of glioma and apparently is not an indication of benignity. In a large number of cases of glioma studied at the Los Angeles County General Hospital, spongioblastomas showed the highest incidence of calcification. The process, however, may occur in any type of the glioma group. Courville and I (Intracranial Calcification, with Particular Reference to That Occurring in the Gliomas, *Arch. Surg.* **21**:801 [Nov.] 1930) made a short report of these cases. We expressed the opinion that calcification is primarily a chemical rather than a histologic process and that while roentgenographic studies of the skull made as a routine may reveal evidence in cases in which tumor is suspected, there are many more instances in which calcification occurs without being demonstrated in the roentgenogram. This may not necessarily be because the films are improperly taken but because the calcareous particles are so small as not to be visualized. In any case, when an intracranial tumor is suspected, it is important to have stereoscopic pictures in which details can be clearly seen, so as not to overlook any evidence of value in the diagnosis.

CEREBROSPINAL FLUID IN DIFFERENTIAL DIAGNOSIS. MARY DAILEY IRVINE, Boston (by invitation).

I present in this paper a more or less chronological survey of work done by me in association with Dr. Frank Fremont-Smith in the department of neuropathology of the Harvard University Medical School in building up a system for differential diagnosis by examination of the cerebrospinal fluid and in substantiating the theory that the spinal fluid is a protein-free dialysate of the blood plasma. This theory was suggested by Mestrezat in 1912. Fremont-Smith (Nature of the Cerebrospinal Fluid, ARCH. NEUROL. & PSYCHIAT. **17**:317 [March] 1927) discussed the theory in detail and presented evidence that the choroid plexus acts as a semipermeable membrane, through which the spinal fluid is filtered as a result of the hydrostatic pressure in the capillaries of the choroid plexus. The series of papers on the equilibrium between the cerebrospinal fluid and the blood plasma present further evidence. It is remarkable how well the variations in the osmotic pressure and the protein, sodium and chloride contents conform to what one would expect on the basis of a Donnan membrane equilibrium, when one considers that only the absolute concentrations of the various substances in the two fluids are known and not the activities.

The influence of a sudden change in the concentration of the blood on the intracranial pressure was first considered. Instances were cited in which a diagnosis of tumor of the brain or of abscess of the brain was dismissed owing to the presence of a normal or a low pressure, when actually the pressure had been lowered just before the puncture by an increase in the concentration of the blood through dehydration resulting from excessive vomiting or diarrhea. This is one example of how findings from lumbar puncture and examination of the spinal fluid may be misinterpreted, if the mechanism which alters these findings is not considered.

The influence of the blood chloride level on the chloride content of the cerebrospinal fluid, as well as the effect of bringing the protein levels of the plasma and the spinal fluid closer together and thereby reducing the ratio of the chloride content of the cerebrospinal fluid to that of the plasma, was next considered as further evidence of the Donnan effect. Low chloride ratios were observed in cases of nephrosis, in which the protein content of the plasma was low, and in cases in which the protein content of the plasma was normal but that of the spinal fluid was extremely high, as is found in the fluid below a tumor of the spinal cord causing complete block. In cases of meningitis the protein content of the spinal fluid is seldom high enough to affect the protein-chloride ratio. In this condition the low content of chlorides in the spinal fluid is due largely to the low amount of chlorides in the serum. A low chloride content of the serum is found associated not only with meningitis but with most acute infections, and in cases of these conditions, as in all instances in which the amount of chloride in the serum is low whether due to fever or to vomiting, the chloride content of the spinal fluid is low. Comparative studies of the osmotic pressure, the chloride and protein contents and the specific gravity of the blood serum and the cerebrospinal fluid, before and after febrile reactions to typhoid vaccine and malaria, indicated dilution of the blood and consequently a low chloride content in association with fever. A diminution in the amount of chlorides in the spinal fluid reflects the chloride level of the plasma.

Changes in the cerebrospinal fluid are also reflections of changes in the sugar content of the blood in most instances. The important exception is meningitis, in which the important factor in lowering the sugar content of the fluid is the local breakdown of dextrose by living organisms. That living bacteria and not the glycolysis due to the presence of cells cause the low sugar content is of diagnostic value in differentiating meningitis from an aseptic meningeal reaction to septic foci in the cranium. In cases of the latter the fluid is sterile and the sugar content normal. A slightly low sugar content of the fluid may be masked by a high sugar content of the blood, so that in borderline cases it is important to know the value for the sugar content of the blood for an exact understanding of the situation.

The abnormal protein content of the cerebrospinal fluid was next considered. An increase in protein is due to cellular disintegration or to the addition of protein from an inflammatory process. One of the earliest responses to inflammation is increased permeability of the regional blood vessels, so that they become permeable to protein. The increase in the protein content of the spinal fluid often found in cases of myxedema is best explained as due to the increased permeability of the blood vessels in that condition.

The value of the determination of the protein content of the spinal fluid in localizing a tumor of the brain was emphasized. Nothing new in this regard has been discovered since the paper presented by Fremont-Smith (Cerebrospinal Fluid in Differential Diagnosis of Brain Tumor, ARCH. NEUROL. & PSYCHIAT. **27**:691 [March] 1932) before the First International Neurological Congress, held at Berne, Switzerland, on Aug. 31, 1931, that is, there is a high protein content of the lumbar fluid with a normal protein content of the fluid from the ventricles in cases of acoustic neuroma and other tumors of the cerebellopontile angle; a normal or slight elevation of the protein of the lumbar fluid with a normal protein content of the fluid from the ventricles in cases of glioma of the cerebellum, and a normal protein content of the fluid from all parts of the central nervous system in cases of tumor of the fourth ventricle and glioma of the pons. In cases of tumor of the third ventricle the protein content is high in the fluid both of the lumbar region and of each lateral ventricle. In cases of tumor of the hemisphere the protein content of the fluid from all regions is normal unless the tumor invades the lateral ventricle or comes extremely close to the wall of the ventricle, in which case there will be a high protein content of the fluid of the ventricle on the same side as the tumor, a normal or only slightly elevated protein content of the fluid of the opposite ventricle and a high protein content of the lumbar fluid. A tumor of the surface of the hemisphere occasionally produces a high protein content of the lumbar fluid, without elevation in the fluid from either ventricle. A tumor of the pituitary gland does not cause an increase in the protein content. There are exceptions, of course, to each of these statements, but in general they form the most intelligent working basis for the use of the spinal fluid as an aid in the diagnosis of tumor of the brain.

The importance of always counting both the red and the white cells in the fluid was stressed, as adequate calculations can then be made for the white cells and the protein added by accidental contamination of the fluid by blood. This procedure has been particularly helpful in examintaion of the ventricular fluid in cases in which a slight increase in the protein content may be of diagnostic significance.

The colloidal gold test is the most valuable of the colloidal tests in general use.

The importance of careful examination of the spinal fluid, which can be carried out easily in any clinical laboratory, has been proved by the fact that of the 6,000 or more specimens of fluid examined each year in the laboratories of the Massachusetts General Hospital and the Boston City Hospital, a large proportion are not from the neurologic and neurosurgical services but are referred by medical and surgical services for aid in diagnosis. Special credit is due Dr. Frank Fremont-Smith for furthering the study of the relationships of the cerebrospinal fluid and the blood from not only a theoretical but a practical standpoint. Owing to his efforts, much material has been collected on the findings in the blood and spinal fluid in a multitude of conditions.

DISCUSSION

DR. EUGENE R. LEWIS: Does an increase in the cell content of the spinal fluid constitute one of the sources of the increase in the protein content of the fluid? The ophthalmologist meets problems of alterations in the osmotic pressure in cases of glaucoma; the otologist meets similar problems in conditions which may be referred to as "labyrinthine glaucoma." In both these there appears to be a relation between the circulatory and the local tension. Is there evidence of a similar relation between the cerebrospinal and the circulatory tension? Is there any

apparent degree of correlation between the chloride and the protein concentration, on the one hand, and the cerebrospinal and the circulatory tension, on the other?

MRS. IRVINE: An increase in the cell content of the spinal fluid does constitute a source of increased protein content, as protein is added to the fluid by the disintegration of the cells. To determine the protein content effective in the fluid when it is withdrawn, one should use the supernatant fluid, if there are several hundred or several thousand cells per cubic millimeter. If one does not do this, one will probably destroy the cell membrane and release protein by the addition of chemicals and so obtain a higher protein content than is actually effective in the chloride-protein relationship.

For a discussion of the relation between the circulatory and the local tension one may refer to the work of Duke-Elder on intra-ocular pressure and the paper of Fremont-Smith on the nature of the cerebrospinal fluid.

Regular Meeting, June 1936

EUGENE ZISKIND, M.D., *President, in the Chair*

NATURE OF THE NEUROTROPIC MICRO-ORGANISMS OF RABIES AND POLIOMYELITIS.

DR. F. PROESCHER, San Jose, Calif.

Pasteur first demonstrated that the causative agent of rabies is observed in pure culture in the central nervous system of animals suffering from rabies, thereby forming the basis for all future investigation. In spite of the extensive work which has been done since, no definite conclusions have been reached as to the nature of the causative agent. Pasteur noted coccoid formations in fresh emulsions from the medulla oblongata of animals with rabies, but he came to no conclusion as to their significance. Similar formations were noted by Bouchard, Roux and Gibier. In 1896 Babes demonstrated fine intraplasmic granules in sections of the central nervous system of animals with rabies with the Cajal silver impregnation method and the Giemsa stain, and he expressed the belief that they represent the active form of the rabies virus. Babes did not mention that he could demonstrate these granules in smears. However, these observations have not been confirmed by other investigators. According to my studies, these granules are either pathologic cell structures or precipitates of silver.

An important discovery tending toward a solution of the etiology of rabies was made by Negri in 1903. With a variety of staining methods he demonstrated peculiar structures in the protoplasm of the large ganglion cells of the cornu ammonis. Negri expressed the belief that these structures were protozoa and the micro-organisms of rabies. All critical investigators have come to the conclusion that the Negri bodies, while of great diagnostic value, represent a cellular degeneration product, which may enclose the rabies virus and are not of a protozoan nature.

In 1910 Koch and Riesling demonstrated coccoid formations in sections of the brain and spinal cord with the Heidenhain iron-hematoxylin and von Krogh stains; they failed to demonstrate the cocci in smears. It is difficult to differentiate cocci and granular degeneration products in pathologically changed brains and spinal cords, and no definite conclusions can be reached as to their significance.

Remlinger, di Vesta and others claimed that the micro-organisms of rabies are filtrable and therefore cannot be demonstrated microscopically. According to Bertarelli, the rabies virus is not entirely filtrable through the Berkefeld filter V, because the filter residue is more virulent than the filtrate. The filtrability of the rabies organism has not been confirmed by either Stimson or myself.

The negative results of the filtration experiments indicate that the rabies organism must lie within the range of microscopic visibility. The difficulty, therefore, in demonstrating the organism in smears or sections with common staining procedures must be due to special staining properties. In carrying out systematic

staining experiments with street and fixed virus it is sometimes possible to demonstrate a large number of small cocci after fixation with mercury bichloride and alcohol and the application of a modified Gram stain. Further investigation revealed that the micro-organism can be stained substantively with certain aniline dyes belonging to the thiasine group, such as methylene azure, methylene violet and toluidine azure. The carbinol base alone is capable of staining the micro-organisms. The majority of the micro-organisms stainable with methylene azure ranged in size from 0.2 to 0.5 micron. The constant presence of this organism in street and fixed virus makes its etiologic relationship to rabies almost certain. The final proof was its artificial cultivation and the production of the disease with distant subcultures. The micro-organism can be cultivated in bouillon, with the addition of ascitic fluid, sheep or rabbit serum and fresh tissue. Inoculation of rabbits and a monkey with distant subcultures produced typical rabies.

The similarity of the biologic properties of the virus of poliomyelitis to those of rabies suggested that it may have the same staining properties. Staining with methylene azure of smears and sections of the brain and cord of man and monkeys with poliomyelitis revealed a great number of small cocci similar to those observed in rabies. Flexner and Noguchi cultivated a small coccus from the central nervous system of man and monkey with poliomyelitis which produced poliomyelitis in monkeys. Microscopically these cocci are identical with those demonstrated in smears and sections with methylene azure. I have cultivated the same micro-organism and produced typical flaccid paralysis in a monkey with the fortieth subculture.

Unpublished staining experiments with victoria blue 4 R have further confirmed my observations in cases of rabies and poliomyelitis. The same micro-organisms are made visible with this dye as with methylene azure. The difficulty in staining the micro-organisms is apparently due to a lipoid protein which can be made visible only with strong basic aniline dyes.

The morphologic characteristics and successful cultivation of the micro-organisms of rabies and poliomyelitis suggest that these organisms in all probability belong to the bacteria.

NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY

Regular Meeting, April 14, 1936

LEON H. CORNWALL, M.D., *Chairman, Presiding*

CYRUS BURNS CRAIG

The members of the Section of Neurology and Psychiatry of the New York Academy of Medicine record their deep sense of loss in the death of Cyrus Burns Craig. Conservative by training and inheritance, he exerted a powerful influence in moderating more extreme views, and his thoughtfully considered opinion was eagerly sought by his friends and associates. His attitude toward matters of policy was invariably one of reason and conciliation. Devoid of any element of personal aggrandizement, his efforts were always directed toward the ultimate good, thus disarming criticism and unreasonable opposition. He gave of himself continuously and unsparingly that the art of medicine and the teaching of the student body might fulfil their highest functions. It might truly be said that his devotion to his task made him ignore his illness in its early stages. Literally, he sacrificed his life for his work. Where courage, ability and patience were required he accepted responsibility. Pleasing in personality, simple and modest in manner, unassuming, friendly and human, he was, nevertheless, a man of strong personality; he never created antagonism or wounded tender sensibilities. His patience in suffering and courage to the end of a long and painful illness paralleled his life of constructive effort.

Dr. Craig bore the heritage of fine ancestral stock. On his maternal side he was a collateral descendant of Robert Burns; a direct ancestor was the famous Alexander Burns, who won distinction at Yorktown, Quebec. Dr. Craig's grandfather, Robert Carroll Burns, was one of the first men in southern Ohio to seek emancipation for the enslaved Negro.

Dr. Craig was born in Ohio and graduated from the College of Wooster, at Wooster, Ohio, in 1907 and from the Western Reserve University School of Medicine at Cleveland four years later. He served an internship first at the Lakeside Hospital in Cleveland and then, in 1912, at the newly founded Neurological Institute of New York, then under the direction of Dr. Joseph Collins. During the World War Dr. Craig served as neurologist with the American Ambulance Corps and saw active service at the front, participating in the battle of the Argonne. He received a commission as captain in the Reserve Corps in 1917. Features of his work in the Department of War were the plans he drew for various types of therapy used in the rehabilitation of disabled soldiers. These plans were immediately adopted at the Walter Reed General Hospital and at Fort McHenry, Baltimore, Md., and were widely reproduced in the Army and other hospitals.

When the Neurological Institute of New York was built, he labored unceasingly for more than two years as the medical member of the Building Committee. In appreciation of his labors, his fellow-members of the medical staff presented him with a silver loving-cup. Dr. Craig was consultant in the building and equipment of the Doctor's Hospital and the New York Ophthalmic and Aural Institute. He also designed the finely equipped physical therapy department of the Neuro-psychiatric Institute and Hospital of the Hartford Retreat in Hartford, Conn.

Combined with his fine qualities, there were a kindliness of spirit, an abundance of human charity and a sweetness of character, which endeared him to his friends and associates. The Section of Neurology and Psychiatry will grievously feel the loss which it has sustained and will miss his influence.

In token of its loss, the section expresses thus its sorrow and its appreciation of Burns Craig, with the hope that its sympathy may lighten the burden of sorrow carried by her who survives him. It is the wish of this committee that this memorial be spread on the minutes of the section and a copy transmitted to the members of his family.

DR. SYLVESTER RICHARD LEAHY

The Section of Neurology and Psychiatry of the New York Academy of Medicine records with sorrow the death of Dr. Sylvester Richard Leahy

Dr. Leahy was graduated from the Yale University School of Medicine in 1905. He served a three year internship at the Bellevue, Willard Parker and Christ Hospitals. In 1909 he entered the New York State Hospital service, serving both at the King's Park State Hospital and the Manhattan State Hospital, and in 1914 he became resident alienist in charge of the psychiatrist division of the King's County Hospital. Here he remained until 1918, when he was appointed captain in the United States Army Medical Corps.

After his military service, Dr. Leahy organized and became the first medical director of the mental clinic of the Catholic Charities.

For many years a member of the medical staff of the New York Police Department, Dr. Leahy won distinction as neuropsychiatrist to the Board of Surgeons. His unquestioned integrity and unswerving loyalty to the best interests of the community gained for him the confidence and esteem of the officers and the men in the department.

In 1922 he entered private practice. From 1922 to 1929 he was clinical professor of psychiatry at the New York University College of Medicine, and from 1922 to the time of his death, assistant attending neurologist to the Neurological Institute of New York.

He was a member of the New York Academy of Medicine, the American Psychiatric Association, the New York Neurological Society and the New York Society for Clinical Psychiatry, of which he was secretary at the time of his death.

The Section of Neurology and Psychiatry of the New York Academy of Medicine wishes to pay tribute to Dr. Leahy's fine character, high professional standards and devotion to duty. He exemplified in his professional life the characteristics of the true physician—a modest approach to the tasks which daily confronted him and the utmost in service to his patients. We mourn the loss of a fine colleague.

Resolved, that this resolution be spread on the minutes of the Section of Neurology and Psychiatry and that a copy thereof be sent to his family.

S. PHILIP GOODHART
HENRY ALSOP RILEY
EMANUEL D. FRIEDMAN

EXTRADURAL LIPOMA COMPRESSING THE SPINAL CORD: PRESENTATION OF A CASE. DR. ANATOLE KOLODNY (by invitation).

A white woman aged 36, who weighed 225 pounds (102 Kg.), commenced to feel numbness in the left foot two years prior to operation. Sixteen months prior to operation there appeared spastic paralysis of both lower extremities and of the abdomen. The bladder and the rectum were involved. After spinal puncture a sensory level corresponding to the sixth dorsal segment appeared. The spinal fluid was normal, and there was no indication of a complete block. Forceful percussion over the sixth and seventh dorsal vertebrae was felt by the patient as "jarring" in both feet. Roentgenograms of the spine revealed normal structure.

At operation the fifth, sixth, seventh, eighth and ninth dorsal laminae were removed. A yellow, dense tumor was extirpated from immediately beneath the laminae. This growth measured 2.5 cm. in width, 1 cm. in thickness and 12 cm. in length. The dura was not involved.

The function of the bladder returned twenty-four hours after operation. When the patient left the hospital, on the fourteenth day after operation, she was able to stand on her feet with support. She has remained well up till this time, over sixteen months after operation.

Histologic examination of the tumor showed a typical lipoma, without round cell or polymorphonuclear infiltration.

A few questions arise in discussing this case. First, why did I consider the tumor extradural rather than intramedullary. Only one point, in my opinion, indicated an intramedullary growth, and that was the existence of the tumor one and a half years before the patient was admitted to the hospital. A tumor that exists so long before it produces paralysis is generally accepted as intramedullary. On the other hand, several points indicated an extradural, or at least an extramedullary, growth: (1) The sensory level appeared clear after lumbar puncture. It was pointed out years ago by Dr. Elsberg that a sensory level which is not clear becomes so after lumbar puncture in the presence of an extradural growth. (2) On forceful percussion over the site of the growth jarring was felt in the lower extremities; in my experience this finding points to an extramedullary or an extradural growth. (3) There were contralateral findings in the early examination. As I mentioned in the history, there were weakness of the lower extremity on the left (contralateral) side and numbness and weakness in the extremity on the same side.

A tumor of this kind is rare. Dr. Stookey, in reporting an instance of intramedullary lipoma several years ago, collected from the literature 9 cases of extradural lipoma. They dated back to 1847. This collection was limited to lipomas not connected with spina bifida. Cases of the latter type, the so-called sacral tumor of Chiari, are frequent. However, cases of extradural lipoma of the spinal canal not in conjunction with spina bifida are rare. Another case of this type has been reported since by Dr. Elsberg and 1 by Drs. J. Kasper and A. Cowan. In all, 11 cases have been reported, mine making 12. In only 2 instances was operation performed. In all the rest the tumor was observed at postmortem examination.

There was no polymorphonuclear infiltration. I mention this because the question was raised by Dr. Sachs several years ago. He stated that such a

lipoma is not a true fat tissue growth but is connected with atrophy around the spine as a compensatory growth. The fact that the tumor in the present case was well encapsulated and demarcated, without unusual fibroblasts or round cell infiltration, points to its being a true lipoma.

DISCUSSION

DR. IRA COHEN: In addition to this rare form of lipoma of the spinal canal, I recall seeing another type in Dr. Elsberg's service, on which he operated. Subsequently, I performed operation on the same patient. The condition is known as *adeno-lipomatose symétrique,* in which the lipomatous deposits are laid down in the region of the lymph nodes. They are symmetrical and involve the axillary, inguinal or cervical nodes. In this patient a similar deposit was observed within the spinal canal. This type of lipoma can be considered malignant. Before the spinal operation, while the patient was on the general surgical service, lipomas were removed on several occasions and recurred. They recurred twice after removal from the spinal canal. This type of lipoma probably is made up of embryonal fat cells, which may account for its malignant character.

LESION OF THE UPPER CERVICAL PORTION OF THE CORD, RESEMBLING COMBINED SYSTEM DISEASE: PRESENTATION OF A CASE. DR. E. D. FRIEDMAN.

In 1926 I reported before this section 2 instances of lesion of the upper cervical portion of the cord in the guise of combined system disease (Friedman, E. D.: *M. J. & Rec.* **126:** 734 [Dec. 21] 1927). Néri (La forme ataxique initiale des compressions médullaires cervicales, *Rev. neurol.* **1:** 60 [Jan.] 1932) reported 3 similar cases. All his patients presented, in addition to the other signs, well defined nystagmus, and a tentative diagnosis of multiple sclerosis was made in each case. The first case was one of melanosarcoma, at the level of from the third to the fourth cervical vertebra. The tumor was placed anteriorly and pushed the cord backward. In the second case a similarly located neoplasm was observed. In the third case the presence of the neoplasm was not verified at operation, but the clinical course strongly suggested such a lesion. It is of interest to note that in the first two cases the nystagmus disappeared after operation. Néri referred to a similar case, reported by Roussy and Levy (*Rev. Neurol.* **1:**145 [Feb.] 1930), in which there was complete preservation of the pain and temperature sense; owing to the presence of sensory disturbances of the type involving the posterior columns and the picture of "cortical anesthesia," operation was erroneously carried out on the brain (parietal lobe). My associate Dr. William Schick (Tumor High in the Cervical Region of the Spinal Cord Simulating Combined System Disease, ARCH. NEUROL. & PSYCHIAT. **32:**1343 [Dec.] 1934) reported a similar case before this section. I now add another case to the group.

REPORT OF CASE

Joseph V., an elevator operator and garage worker aged 32, was admitted to the neurologic service of the Bellevue Hospital on Nov. 27, 1934. His family history was without significance. Herniotomy had been performed three years prior to his admission to the hospital, and a gonorrheal infection occurred at the age of 26. The present illness was said to have begun gradually in December 1933, about one month after an attack of grip, when he noted numbness in the tips of the fingers of the right hand. In August 1934 there was weakness of the right arm, which grew progressively worse. In September 1934 he noted weakness of the right leg; in October, paraesthesias of the left hand, and in November, weakness of the left arm. A month later he noted weakness of the left leg. His gait became somewhat stiff, and there was increasing difficulty in locomotion. Since July 1934 he had experienced urgency of urination but no incontinence or retention of urine. There was no disturbance in potency. He had no visual difficulties, but there was slight impairment of hearing. There was no history of remissions or exacerbations.

Neurologic examination showed normal pupils and pallor of the temporal halves of the disks, with 20/25 vision in each eye. Horizontal nystagmus was present, chiefly to the left. The right palpebral fissure was somewhat wider than the left, and the jaw jerk was active. The other cranial nerves showed no deviation from the normal. There was quadriparesis, with hyperactivity of the deep reflexes; spasticity, more pronounced on the right; absence of abdominal reflexes; ankle clonus, and Hoffmann and Babinski signs bilaterally. There was slight intrinsic atrophy of the hands (?) but no fibrillation.

Sensory examination suggested the presence of a level for pain sense at the fourth cervical vertebra, but temperature and tactile sense were not strikingly altered. There was another level on the right at from the seventh to the eighth dorsal vertebra, below which a pinprick was not so acutely felt as on the left. Temperature and tactile sense were not seriously disturbed, and the sacral zone was "spared." Sensation involving the posterior columns (vibration, position and two-point discrimination) was lost practically up to the shoulder. These disturbances were accompanied by astereognosis, tabetic athetosis and ataxia, especially on the right. No immobilization of the head was noted. There was no history of cervical pain, with radiation into the shoulders. No tenderness over the cervical portion of the spine was elicited on percussion. There was no band sensation about the neck, but a feeling of tightness in the middorsal zone was noted.

Fluoroscopic study of the diaphragm showed no abnormalities. The Wassermann reaction of the blood was negative. Gastric analysis revealed the presence of free hydrochloric acid, and examination of the blood yielded normal results. The spinal fluid was clear and colorless and showed a total protein content of 60 mg. per hundred cubic centimeters, and manometric readings suggested block. There were 2 cells per cubic millimeter. The Wassermann and colloidal gold reactions were negative.

The clinical impression was either infectious myelitis or atypical disseminated sclerosis, with concomitant arachnoiditis. The belief was expressed that tumor of the cord would have to be ruled out by subsequent observation. To complicate the situation further, lead was found in the urine. Because of the signs suggesting a sensory level, the slight evidence of block of the cerebrospinal fluid and the protein content of 60 mg., an exploration was made by means of bilateral laminectomy, extending from the first to the fifth cervical vertebra. A tumor, about the size of an English walnut, placed extradurally and ventrally, was observed on the right, at the level of the sceond cervical vertebra. There was a small intradural extension. This was removed. The dura was opened for a short distance, in order to make certain that no part of the tumor had been left within the dura.

The microscopic diagnosis was meningeal fibroblastoma. The patient made an uneventful recovery. He was discharged from the hospital on March 7, 1935.

Reexamination on March 12, 1936, revealed a few nystagmoid jerks in the horizontal plane and a somewhat narrowed palpebral fissure on the left but no other signs of the Horner syndrome. There was no motor weakness. The deep reflexes were a little more active on the right. The abdominal reflexes were absent on the right and present on the left. The Hoffmann, Babinski and Rossolimo signs were not elicited. No sensory changes could be demonstrated. There were no symptoms of bladder disturbance. The patient has been working since his discharge from the hospital.

This case illustrates the symptom complex already described. The upper level of the disturbance in pain sense occurred in the so-called indeterminate zone between the fourth cervical and the second dorsal vertebra. It was not clearcut or sharply defined. There were no atrophies or fibrillations about the shoulder girdle. The contrast between the severe disturbances in posterior column or gnostic sensation and the relatively mild impairment in pain and temperature sense (vital sensation) forms a striking part of the clinical syndrome. On the occasion of my first presentation of this syndrome, I offered an explanation of this discrepancy by reference to the phylogenetic point of view. The posterior columns are, phylogenetically speaking, a relatively recent acquisition; they first appear in reptiles. In accordance with the point of view of the Dutch school, phylogenetically recently acquired pathways are more vulnerable. It is for this reason that one finds serious implica-

tion of these pathways for gnostic sensation, with relatively little involvement of the spinothalamic fibers, which carry vital sensation; the latter tracts do not become involved in this syndrome until late in the course of the lesion. The recession of signs following laminectomy for tumor of the cord also seems to bear out the phylogenetic point of view. The first pathways to regain their function are the spinothalamic tracts, while the posterior columns and the pyramidal tracts recover function much later. The Babinski sign may persist even for months after complete extirpation of a neoplasm.

It is important also to stress that the suboccipital space is large. I have demonstrated this fact both by actual observation of the operative field and in the clearcut films of this area taken in the course of my work on encephalography. Hence there is plenty of room for a tumor of the cervical region to grow before it exerts pressure on the cord.

I wish also to stress that, contrary to the usual occurrence in cases of extradural tumor, there was no sharper accentuation of the sensory level after lumbar puncture and to say further that, contrary to the usual involvement of the sacral segments in cases of extramedullary compression, sensation in the sacral zone was intact in this case. In my experience "sparing" of the sacral region is characteristic either of intramedullary disease or of anteroposterior compression of the cord, while in cases of side to side compression the sacral areas are involved first, owing to the peripheral location of the sacral fibers in the spinothalamic pathway.

It may be that the ventral location of the neoplasm was a factor of importance in this case and that the posterior columns were involved because of their dislocation posteriorly, with resulting contrecoup pressure on these pathways.

DISCUSSION

DR. FOSTER KENNEDY: A number of important ideas emerge from Dr. Friedman's presentation. First, his statement regarding the phylogenetic youth of the posterior columns: These columns seem enormously vulnerable; I think they are the most vulnerable part of the spinal cord. Appreciation of their early implication in almost any disease, whether toxic or compressive, will aid much in diagnostic acumen. As a house physician, I remember seeing a patient in whose case a diagnosis of tabes was made at first. He had a completely tabetic gait, with no sense of vibration or of position in the feet. A tumor of the spinal cord was successfully removed. I watched the recovery; function came back in the same order in which it had gone; that is, about two, three or four months after the operation—I have forgotten how many—the patient again had a tabetic gait; from this condition he finally emerged. The posterior columns were finally restored. They were the first to be implicated by the compression of the tumor and the last to recover. These columns, because of their phylogenetic youth no doubt, are the first to be involved in a case of subacute combined sclerosis of the cord. I remember George Minot telling me that if he had the choice of a blood-counting chamber or a tuning fork with which to make a diagnosis of pernicious anemia, he would prefer the tuning fork, for he was sure that it furnished the most complete evidence of subacute combined sclerosis of the cord, in which the loss of vibration sense is the first sign of involvement.

The next lesson to be learned from this case is the significance of bilateral astereognosis. Bilateral astereognosis is not uncommon; it is usually thought to be a cerebral state, due to a cerebral lesion. That is the first idea that comes into the mind of most persons. Dr. Friedman described a germane case, which is almost a replica of one which, as he probably will remember, was shown by Dr. Harvey Cushing at the meeting of the American Neurological Association, at Boston, ten or twelve years ago. A patient with evidence of tumor of the brain had astereognosis in the left hand. On the basis of this finding, Cushing opened the right parietal area and saw nothing; being one of the greatest surgeons in the world, he was able to close the operation without doing the man harm. Perhaps he made him better. As symptoms developed, however, it grew clear that the patient had a tumor of the left half of the cerebellum. Cushing removed a tumor from this area, from which operation the patient recovered. He presented the patient at a meeting, about two months afterward, as having astereognosis

caused by a cerebellar lesion; the whole meeting was thoroughly upset. All barked furiously that a lesion of the cerebellum cannot cause astereognosis, but they could not prove it. I examined the man the next day and found no vibration sense in the left arm. The condition really was localized high tabes, caused by stretching due to a cerebellar tumor. Involvement of the posterior roots in the upper cervical region frequently leads to astereognosis in one or both hands, and this sign is, I believe, almost diagnostic of a lesion in that area.

The third lesson to draw from this case is the attitude to be adopted toward spinal disease with regard to surgical procedure. I have almost laid aside any mind I ever had in regard to spinal disease in that I have come often to be content in such a condition to say whether or not an opening is to be made. I think that this is the important attitude of mind to have in regard to spinal disease. One must decide: Is this a condition to be treated with surgical means, or is it not? Whether a patient is suffering from this or that particular ailment of the spinal cord is usually an academic point, but it is by no means academic that, if one has the feeling one can put his finger on the level of the lesion, one should give the patient the advantage of surgical inspection of that part. I think that any other attitude is not fair to the patient. The patient should be allowed to have the advantage of modern neurologic surgical treatment, which is now so good that opening the spinal canal is no more hazardous than opening the abdomen. If one thinks one knows where the lesion is in the spinal cord, unless one knows that the situation is medical—and one rarely knows that—one should allow the patient to have the area inspected.

Dr. E. D. Friedman: I am obliged to Dr. Kennedy for stressing the instructive features of this case. Every neurologist must agree with his statement concerning the vulnerability of the posterior columns. They are involved early in tabes, multiple sclerosis and combined sclerosis.

I forgot to speak of the nystagmus in this case. The slight temporal pallor of the disks was not accompanied by the presence of scotomas. A case for the diagnosis of multiple sclerosis, however, could easily be made. Serko, I believe, first described nystagmus in cases of tumor of the cervical region of the cord. He described a case in which he demonstrated nystagmus in association with a tumor of the cord even as low as the upper dorsal zone. One must, therefore, bear in mind that the presence of nystagmus does not militate against the diagnosis of a level lesion of the cord.

I was glad to hear Dr. Kennedy say what he did about astereognosis. In one of Strümpell's last papers, he stressed that the concept of astereognosis as formulated by Wernicke (namely, loss of gnostic sense without objective sensory disturbance) can no longer be maintained. This symptom can be demonstrated in disease involving the fibers of the posterior columns anywhere between the parietal cortex and the posterior roots.

The present case further illustrates a nice point in diagnosis stressed by Oppenheim when he divided spinal hemiplegias into "upper" and "lower" types. With a lesion above the fifth cervical vertebra there is likely to be spasticity of both limbs on the involved side, whereas with the lesion below this point there is likely to be flaccidity of the upper extremity and spasticity below. My case bears witness to the clinical truth of this observation.

With regard to Dr. Kennedy's advocacy of surgical intervention in cases in which signs even suggesting a level lesion are presented, one can only say a strong word of approval, for exploratory laminectomy today is a safe procedure and occasionally one uncovers a surgically removable condition.

Dr. Henry Alsop Riley: I do not wish to push my point of view unduly, but I believe that if the term astereognosis is to have any value it must be understood that the term is used with certain limitations and as a definite concept. I had occasion about two months ago to take this exception to a similar, as I believe, misuse of the word which Dr. Kennedy and Dr. Friedman have expressed tonight. I wish to ask Dr. Friedman and Dr. Kennedy what their definition of astereognosis is. To my mind the term astereognosis should be limited to the inability to recognize the form and character of an object by the use of the body senses

unaided by the special senses, and the primary sense qualities of touch, pain, temperature, vibration and movement must be relatively intact before one can speak of astereognosis. This concept of the term eliminates the loss of appreciation of the identity of objects due to nerve disturbances, disorders in conduction in the sensory tracts of the spinal cord and lesions in other vicinities which may interfere with the proper conduction of the primary sense qualities. If the patient is unable to synthesize these relatively intact primary sense qualities into the elaborations which, I believe, depend on cortical activity and if he shows loss of two point discrimination and inability to recognize and localize a point stimulated and to appreciate weight or form, then in my opinion, one can speak of astereognosis. If the term as such is to have any value, its use should be so delimited. If it is to be used in cases in which marked changes in the primary sense qualities are shown, one should speak of these disturbances as such and not of astereognosis. The term astereognosis infers cortical activity and depends on the elaboration and synthesis of the preliminary sense qualities and their comparison with past and present experiences. I believe that these processes are cortical, since they depend on memory, and that the lower centers so far as consciousness is concerned have no particular memory functions. I believe that there is a distinction between the ability to recognize movement and the appreciation of positions and attitudes. These again depend on memory comparisons and are cortical. Comparisons of past similar or dissimilar situations with present conditions cannot be carried out without intact primary sense qualities. To do this requires the activity of the cortex, namely, that of memory and comparison. If the situation is reduced to the absurd, a patient without a hand cannot appreciate form and therefore, according to the loose use of the word, has astereognosis. The part of the word consisting of the term "gnosis" connotates cortical activity, and therefore the use of the term for disturbances involving lesions situated subcortically is, to my belief, incorrect. If the word is to be made so meaningless as to represent the loss of the ability to recognize form—no matter from what cause—the term loses its fundamental value.

DR. FOSTER KENNEDY: You do not mean that astereognosis cannot arise from a lesion of the spinal cord?

DR. HENRY ALSOP RILEY: I know that inability to recognize the form of an object can result from a lesion of the spinal cord, of the medullary nuclei and of the thalamus, but with lesions in these situations there is usually marked, if not profound, interference with the preliminary sense qualities. The term "stereo-anesthesia" has been suggested for this situation, leaving astereognosis for the disturbances the cause of which is situated at a higher level.

DR. FOSTER KENNEDY: I think the term astereognosis ought to be used with reference to loss of the faculty of knowing and recognizing an object held in the hand.

DR. HENRY ALSOP RILEY: It seems to me that the condition of the primary sense qualities distinguishes between the terms stereo-anesthesia and astereognosis. If they are intact or relatively so, the term astereognosis can be used. If not, the term stereo-anesthesia is applicable. The term astereognosis should be limited to disturbances in the parietal lobe.

DR. E. D. FRIEDMAN: I think that if Dr. Riley will review his cases carefully, he will find that astereognosis cannot exist without disturbances in the particular type of sensation which is carried by the posterior column. One can demonstrate astereognosis in the sense in which Dr. Kennedy has defined it in cases of lesion of the parietal lobe, thalamic disease, compression of the cord, multiple sclerosis, combined sclerosis and polyneuritis. I do not think the symptom can exist without implication of this particular pathway.

DR. LEON H. CORNWALL: Does Dr. Riley suggest any term to designate loss of the ability to recognize form when this is associated with accompanying impairment of one or more of the primary sense qualities, other than the terms already in use which apply to disturbances of the primary sense qualities?

DR. HENRY ALSOP RILEY: I do not know of any terms which describe disturbances in the primary sense qualities except the statement that there are disturbances in such and such modalities. If these sense qualities are intact and there is still inability to perceive form, texture, weight and the like, then and only then can one use the terms generally accepted as indicating disturbances in the cortical sensibilities, such as astereognosis, baragnosis and topagnosis.

TORULA INFECTION OF THE CENTRAL NERVOUS SYSTEM. DR. S. PHILIP GOODHART AND DR. CHARLES DAVISON.

Torula infection of the central nervous system is a rare clinical entity, not often diagnosed and occasionally discovered at autopsy. Careful search of the spinal fluid will reveal the organisms. About 50 cases of this infection have been studied histologically. Two thirds of the reported cases were from the United States. Men are more frequently afflicted. The duration of the disease is from one to sixteen months. Infection is probably by way of the respiratory tract. The prodromal symptoms are as variable as those of tuberculous meningitis: Signs of disease of the upper respiratory tract and especially of pulmonary tuberculosis, sinusitis, otitis media, mastoiditis, enlargement of the lymph nodes, general myasthenia, insomnia, headache and torpor have all been described. Some authors deny the presence of prodromal symptoms in the cases observed.

The early clinical features are headache, becoming progressively more constant and severe, with associated nuchal rigidity and pain, nausea and vomiting, often projectile. Amblyopia, diplopia and mental changes suggest organic disease of the brain. Tuberculous meningitis is often the diagnosis made during life. Paresis or paralysis of hemiplegic character is present, and occasionally convulsive seizures occur. In some cases no symptoms involving the nervous system are observed; again, the only suggestion of central involvement may be loss of memory and personality changes. Most commonly, the symptoms point to meningitis and associated involvement of the cranial nerves. Hemiparesis, aphasia and central blindness have also been recorded. Neuroretinitis, papilledema and choked disk occur approximately in 2 of 3 cases, and instances of diplopia, anisocoria, rigidity of the pupils and nystagmus are recorded. The diagnosis of tumor of the brain has caused a number of patients with Torula infection to submit to operation. The course is usually progressive. During the course of the illness fever may occur, and a high leukocyte count has been reported. Complications noted are abscess and cirrhosis of the liver, pulmonary tuberculosis and lymphadenopathy. The spinal fluid findings are the most important in the recognition of the disease. In all but 2 instances in which manometric readings were determined, there was increase in the cerebrospinal pressure to as high as 700 mm. of water. Although the fluid is at times clear, it is usually slightly cloudy and sometimes definitely so. The appearance may vary from time to time, at first being clear and later turbid or yellow or even gelatinous. In some cases, after centrifugation or on standing, a pellicle forms. The cell count varies from the normal to a marked increase in the number of cells—from several hundreds to thousands. Often the torula cells which are seen in the spinal fluid are reported as red cells. Red cells observed in a specimen of spinal fluid which was not bloody on removal should always be suspected of being Torula organisms. In about one half of the 50 cases the organism was observed and cultivated during life. The other cells observed in the spinal fluid are lymphocytes and polymorphonuclear leukocytes and occasionally endothelial cells. The specific gravity is about 1.008. There is an increase in the globulin and albumin contents of the fluid, and sugar may be absent. The colloidal gold curve shows partial precipitation in the middle zone and a curve characteristic of dementia paralytica in some cases. The Wassermann and the Kahn reaction are negative. In only 2 cases have the organisms been cultivated from the blood during life. Cultivation of the organisms from the pharyngeal exudate has been made in a few instances.

The disease has invariably been fatal.

The most successful symptomatic treatment is lumbar puncture. After this procedure, as the result of release of intracranial pressure, there are prompt relief of headache and improvement in the mental state. Spinal drainage, daily or oftener, has prolonged the lives of patients. Shapiro and Neal favored a highly nutritious diet—as much as 5,000 calories a day.

REPORT OF CASES

CASE 1.—M. U., a man aged 63, who was admitted to the Montefiore Hospital on Feb. 9, 1933, in the spring of 1932 had had periodic attacks of weakness of the lower extremities and falling while walking. In the summer of that year there developed tremor of both hands, and in December the attacks of falling became more frequent; personality changes also developed, characterized by irrelevant remarks, loss of interest in the surroundings and gradual impairment of memory. In February 1933 the patient became incontinent. The past and the personal history were without significance, except that the patient had suffered from insomnia for two years prior to his death.

General physical examination gave essentially normal results. Neurologic examination disclosed dulness, confusion and disorientation and loss of memory, judgment and insight. Answers to interrogations were delayed and irrelevant; the attitude was that of indifference, without proper emotional tone; the aphasic status could not be determined because of the patient's mental state. There were slight intention tremor and fine tremors of the hands and fingers bilaterally and cogwheel rigidity in all extremities. All deep reflexes were exaggerated, more on the right than on the left, with diminution of the abdominal reflexes and absence of the cremasteric reflex on the right; the plantar response was of extensor type on the right. The mental state was such as to make unreliable a conclusion as to the sensory response. Examination of the fundi disclosed no pathologic changes. There was weakness of the lower left part of the face. The voice was hoarse (meningeal involvement of the medulla oblongata). There was incontinence of urine and feces (since February 1933).

The spinal fluid on March 27 had an initial pressure of 124 mm. of water, without evidence of block; the final pressure, after removal of 10 cc. of clear fluid, was 60 mm. of water. The fluid was clear and colorless and contained no cells. The Pandy reaction was strongly positive; the total protein content was 47 mg. per hundred cubic centimeters on one occasion and 64.2 mg. on another. The gum mastic curve was 1444421000, and on another occasion, 0442100000. The Wassermann reactions of the blood and the spinal fluid were negative. An encephalogram disclosed marked dilatation of the lateral ventricles; the third and fourth ventricles were not well visualized.

The patient's condition became worse shortly after his admission; tremors and drowsiness became more marked. Vomiting, convulsive seizures, deep stupor and general rigidity, with marked cogwheel phenomena, featured the terminal period. Ten days before his death, on March 31, there developed pyrexia, with bronchopneumonia.

The clinical diagnosis was diffuse cerebrovascular sclerosis, with mental changes. The possibility of cerebral neoplasm was considered.

CASE 2.—R. W., a woman aged 25, who was admitted to the Montefiore Hospital on Aug. 30, 1934, in January 1929, during the eighth month of pregnancy, had had a cold in the head, which was followed by mastoiditis. Three days before childbirth mastoidectomy was performed; she made an uneventful recovery. In 1932 she suddenly experienced severe cramplike and labor-like pains in the lower extremities and the umbilical region, which were followed by incontinence of urine. She was taken to the Bronx Hospital, where it was stated that she passed a stone; she remained there for three days. Later in 1932 she consulted a physician for the relief of incontinence and amenorrhea. At that time the presence of a neoplasm of the cord was suspected by a competent neurologist. Spinal fluid findings at this time showed no evidence of block. An operation in 1933 revealed no neoplasm. In March 1934 paralysis of the legs developed suddenly; another

operation was performed, but, again, no tumor was discovered. In June 1934 the patient had what was described as a "spell," associated with a sensation of imminent death; she screamed and became disoriented for from two to three hours; after this experience she complained of dizziness and headache. In August 1934 vomiting occurred after taking food and was at times projectile. Later in the same month she had a seizure characterized by tremor of the entire body, rigidity and grinding of the teeth and, again during this period, was disoriented. Two days later a similar attack occurred during the day, followed by three others of the same nature in the evening. The eyes rolled to the left during and after the attack. These seizures were characterized by headache in the occipital region, vertigo and numbness in the hands and forearms, and in a few attacks there were periods of unconsciousness for about five minutes. A careful history disclosed that these attacks had occurred on an average of once in six weeks from 1931 to 1933. During this period the patient was generally weak and drowsy and experienced a feeling of exhaustion. The condition was described as almost constant.

On her admission to the Montefiore Hospital the patient complained of dizziness, a peculiar sensation of warmth in the feet and aching of the lower extremities. She experienced an odd illusion of objects projected into the distance and manifested incoherence of expressed ideas. At times she was confused; after a seizure on one occasion she regarded her husband as her brother. She had amaurosis for two days and blurring of vision at times.

Physical examination disclosed the presence of numerous sibilant râles throughout the chest and from medium to fine moist râles at the base of the left lung posteriorly.

Neurologic examination disclosed: slow, hesitating nasal speech, approaching the scanning type; complete loss of power and trophic changes in the lower extremities, with no atrophy or fibrillations; flaccid paraplegia, with absence of deep reflexes but with massive spontaneous movements and active abdominal reflexes; bilateral hyperreflexia in the upper extremities, with a suggested Hoffmann sign on the right; tremor and ataxia in the finger to nose and finger to finger tests bilaterally and past pointing on the right; slight dysdiadokokinesis; complete loss of all forms of sensation below the tenth dorsal segment, and Horner's syndrome on the right. The left pupil was larger than the right; both reacted to light and in accommodation; there was pallor of the temporal portion of the right disk, extending partly to the nasal side of the disk, also pathologic pallor of the entire left disk, except for a lunar strip on the nasal side. There was also horizontal nystagmus on lateral gaze. Vesical incontinence developed. The patient was apprehensive and depressed, frequently confused and emotionally unstable.

Course.—There was no change in the course of the disease until Sept. 10, 1934. From this date, at irregular intervals, there occurred seizures of paroxysmal pain in the abdomen, with fever, chills and abdominal tenderness on pressure, but no rigidity. In December 1934 the patient became disturbed, noisy and emotionally upset, with episodes of uncontrolled sobbing and laughter. These seizures were followed by convulsive phenomena, which began as a fine tremor of the left hand and then involved the left forearm and arm and the left side of the face and then the right side of the face and the right upper extremity, with turning of the head and the eyes to the left. During these attacks the pupils were equal but dilated and did not react to light. The reflexes of the left upper extremity were hyperactive. The respiration was irregular, slow and deep. The patient was disoriented as to time and place and begged to "be forgiven." Uremic coma developed and she died on Jan. 6, 1935. She had had no chills since Dec. 18, 1934.

Laboratory Data.—The blood count and differential count were normal; the Wassermann reactions of the blood and the spinal fluid were negative. A spinal tap on Sept. 11, 1934, yielded xanthochromic fluid, which contained many red cells and coagulated spontaneously. On October 3 the spinal fluid was colorless and contained 22 cells, all of which were lymphocytes. The total protein content was 44.4 mg. per hundred cubic centimeters. On both occasions the fluid was under low pressure. The Wassermann and the Kahn reaction were negative, and the

gum mastic curve was 0000000000. On December 24 the urea nitrogen content rose 82.9 mg. per hundred cubic centimeters, and the sugar content of the blood was 126 mg. Prior to this the urea nitrogen content was about 22 mg.

Roentgen examination of the spine showed evidence of a previous laminectomy, involving the eleventh and twelfth dorsal and the first, second and third lumbar vertebrae. Iodized poppy-seed oil was scattered throughout the spinal canal, from the level of the eleventh dorsal vertebra to the cul-de-sac.

The clinical diagnosis was multiple sclerosis and myeloradiculitis.

This case is of unusual interest because of involvement of the spinal cord. Cases in which the parenchyma of the cord is affected are rare. Granulomatous involvement of the spinal meninges was noticed, and in the case of Smith and Crawford there was actual invasion of the parenchyma. In the present case there was definite proliferation of the smaller vessels of the cord and granulomatous structures were observed in the cord proper.

Histopathologic Observations.—In the first case thickening of the meninges was extensive at the base of the brain, and less marked over the cortex. The entire ventricular system was dilated. Gelatinous collections were observed between the right temporal pole and the orbital convolutions and in the right island of Reil. Microscopically the thickened meninges were infiltrated with lymphocytes, endothelial cells, giant cells and numerous torulas. The gelatinous material appeared as an amorphous substance. The cortical zones were slightly infiltrated, and the choroid plexus in the region of the pons was the seat of the same pathologic process.

In the second case, except for the absence of gelatinous material, the pathologic process was similar. In this case there were, in addition, numerous granulomatous collections in the brain, pons and cerebellum. The spinal cord at the tenth dorsal segment was completely demyelinated. The meninges at this level and at other levels of the cord were thickened. The posterolateral arteries showed perivascular infiltrations, with a few torulas. The cord proper contained granulomatous collections, with torulas. There was proliferation of the intraspinal vessels.

DISCUSSION

DR. HENRY ALSOP RILEY: I find it difficult to discuss this paper by Dr. Goodhart and Dr. Davison, for there is nothing in the situation on which to take hold. There is seemingly no avenue of approach from either the clinical or the diagnostic standpoint. As Dr. Goodhart read the two histories, I tried to follow the development of the situation and reached the same diagnosis as he did in each case, that is, diffuse arteriosclerosis in the first case and multiple sclerosis, in the early stages at least, in the second. I think that, certainly, the picture in the second case is that of a disseminated condition, and I find little to criticize in the diagnosis in the first case. Most observers would have been somewhat skeptical of a diagnosis of multiple sclerosis in the second case, but I do not know that there is anything which pointed to the proper diagnosis.

I wish to ask Dr. Goodhart and Dr. Davison two or three questions: (1) What is the usual portal of entry of torula infection? (2) Can Dr. Goodhart, from a review of the literature and his consideration of these two cases, develop any symptom picture which would lead one to the proper diagnosis in the same clinical situation in the future? (3) Is there any safeguard which one can put on an examination of the cerebrospinal fluid which would result in the discovery of something of diagnostic significance in torula infection? (4) In view of the extensive meningitic reaction, how does Dr. Goodhart explain the absence of pleocytosis or of increase in the globulin or the protein content of the fluid?

DR. S. PHILIP GOODHART: As to Dr. Riley's first question about the portal of entry: This and most of the other questions he put are answered in the part of the paper which, because of its length and the extensive program, I did not read. The portal of entry is probably the respiratory tract. This is not definitely known, but it is the conclusion of most observers that the organisms enter through

the pharynx, the tonsils or the lungs. The lymph nodes are apparently the most effective barrier against invasion of the organisms. In many cases a diagnosis of tuberculous meningitis has been made.

The symptoms which lead to an early diagnosis are few. They are merely those of a general constitutional nature, such as one would expect as the result of an infection of this kind. The diagnosis is rarely made during the life of the patient.

As to pleocytosis: I think there is no intense and extensive involvement of the meninges. The condition is doubtless much the same as that in tuberculous meningitis, with which this pathologic condition has some analogy. That is why one so often observes absence of pleocytosis in torula meningitis.

The other questions I will leave for Dr. Davison to answer.

DR. CHARLES DAVISON: I do not know whether there is a definite safeguard in the examination of the cerebrospinal fluid. The only suggestion I can make is that the presence of red cells in a specimen of clear spinal fluid, which was not bloody on removal, should arouse suspicion of torula infection. Under such circumstances, a culture, especially on Sabouraud's medium, will permit the growth of the fungus. In the second case a spinal tap on one occasion revealed xanthochromic fluid and many red cells, and the fluid coagulated spontaneously. The presence of the red cells in the spinal fluid was considered to be due to injury of a blood vessel. If a culture had been made of this fluid the torula might have been demonstrated.

In regard to the absence of increase in the protein and the globulin content: These substances are usually increased, even though the spinal fluid may appear clear. In the first case the Pandy reaction was strongly positive, and the total protein content was 47 mg. per hundred cubic centimeters on one occasion and 64.2 on another. In the second case the total protein content was not evaluated when the fluid was xanthochromic, as it was believed that the fluid was bloody. On another occasion in which the fluid was colorless and contained 22 cells, the total protein content was only 44.4 mg. per hundred cubic centimeters.

DR. HENRY ALSOP RILEY: The fluid obtained on the second occasion was clear, was it not? The 44 mg. of protein is not enough to arouse suspicion.

DR. CHARLES DAVISON: That is exactly what happens in cases of this infection. During the process of infection the fluid may be turbid and may even coagulate and form a pellicle, as in tuberculous meningitis. At other times in the same case the fluid may be colorless and show no increase in the number of cells. It is true that 44 mg. of protein is not enough to be of significance, but on one occasion the spinal fluid was xanthochromic, and there must have been an increase in the amount of protein.

DR. SIDNEY W. GROSS: I have seen two patients with torula infection of the central nervous system. In the first, who was on the service of Dr. Ernest Sachs in St. Louis, the clinical picture resembled that of tumor of the brain; a ventriculogram was made, and craniotomy was carried out subsequently. The lesion was recognized only after microscopic studies. However, after the diagnosis, lumbar punctures were made, and, although the fluid was clear, torula fungi were easily demonstrated in cultures on Sabouraud's medium.

In the second case the picture was much like that of tuberculous meningitis, except that the patient had remissions during which all signs of meningeal irritation disappeared. In this case also torula fungi were grown from the culture of spinal fluid on Sabouraud's medium.

DR. LEON H. CORNWALL: In 1926 Dr. McKendree and I (Meningo-Encephalitis Due to Torula, ARCH NEUROL. & PSYCHIAT. **16**:167 [Aug.] 1926) reported a case of torula infection. The organisms were recovered from the spinal fluid on examination. Other examinations could not be made. In a review of the literature at that time, we found that most writers emphasized the difficulty of finding torulas in the spinal fluid. Often the organisms were seen only once, after many examinations of the spinal fluid. If the spinal fluid was cultured in all cases and the cultures were incubated for at least five days before being discarded, the organisms might be isolated more frequently.

BEHAVIOR PROBLEMS IN CHILDREN OF PARENTS WITH PSYCHOSES AND CRIMINAL HISTORIES. DR. LAURETTA BENDER.

Sixty children who had a psychotic or a criminal parent with an institutional record were studied at the Bellevue Hospital. Evidence of constitutional or hereditary factors was meager and occurred in the case of only a few children of parents with schizophrenia. One child with schizophrenia had a mother with the disease. There seemed to be a type of deviation from the schizoid personality which may have been constitutional. The behavior problems appeared to result from the effects of the loss of the psychotic or criminal parent, the broken home, the unsuitable treatment of the child by the parent or the disturbance in parent-child relationships in the critical periods of the development of the child's personality. Mental and emotional retardation occurred in children who were confined with a parent of defective or schizophrenic personality and were deprived of the normal environmental stimuli for growth. Psychopathic reaction types developed in children who had been deprived of normal home life in the first five or six years of life, before the personality had developed. Neurotic behavior problems arose in children who had been deprived of part, but not all, of the normal home life and parent-child relationships and who were forced to struggle with exaggerated feelings of inferiority, guilt, insecurity and anxiety. Conduct disorders occurred in children who were forced to run away from an unfavorable home and had taken part in associated delinquencies, such as stealing and truancy, and who had bad companions.

In general, there were more behavior problems in children of psychotic mothers than in those of psychotic fathers. There is a group of boys who show serious behavior disturbance as a result of psychosis or criminal conduct in the father. These are boys in whom there develop distorted identification processes in connection with the father when the father, for example, reacts to paranoid delusions, especially against the mother, in the early years of the boy's life, when he normally identifies himself with the father and passes through the Oedipus stage. Such behavior closely patterns the father's psychosis but is associated with an ambivalent attitude toward the father, the mother and the self, with marked emotional instability and serious behavior difficulties. Similar disturbances in personality may occur in a boy whose father shows criminal behavior and is caught and imprisoned or killed for the crime and may appear at the same age in the child as that just described.

In general, behavior difficulties in the children become most serious in early puberty, although the disorder in the parent occurs earlier in the life history of the child.

In the 60 families studied there were 195 living children. Besides the disturbances in the 60 children who were included in this report, there were recorded behavior difficulties in 31 siblings, making a total of 91 children with behavior difficulties, or 44 per cent of the entire number.

The opportunity was used to consider children's concept of mental illness. Their attitude is highly objective. In general, they believe that mental illness is due to violence, especially to blows on the head, and that it is characterized by unwarranted aggression against the child and by cursing.

DISCUSSION

JUSTICE JACOB PANKEN (Domestic Relations Court): The problem which Dr. Bender has discussed comes close home to me because many of the children whom she has studied were referred by the court for study at the Bellevue Hospital. In addition to the cases referred to the hospital for study, the court has its own psychiatric clinic, where studies are made of children who are brought into court, sometimes as neglected and sometimes as delinquent children.

I do not know whether Dr. Bender includes a study of a boy aged about 10 years whom I sent to her. He killed a girl aged 5 years, and when the child was brought to me, I was confronted with what seemed an insoluble problem. Investigation in the court disclosed that the father had had syphilis for about twenty-

five years and that the mother had been infected by the father. I think there were 8 stillborn children. Strangely, an older sister of the boy was not abnormal. Dr. Bender and I discussed the problem of the child at length. Unfortunately, under the provisions of the law, the court cannot remand children to the city hospitals for more than thirty days; hence, this child was remanded for periods of thirty days during about six months. He seemed to "adjust." I do not like that term; I do not like to have children, or even adults, "adjust." I want to know first to what they adjust themselves before I accept the adjustment as worth while. This boy did well for four or five months and then broke out. I hoped Dr. Bender would discuss that case. Ultimately the child went to an institution that cares for mentally sick children.

I remember another case in which 3 children were involved. One child was a Negro, and 2 were Italians. They had stolen a gun from a police officer and started to become gangsters. They traveled along a road and met a young woman. One boy pointed the gun at her and ordered her to hold up her hands. She merely slapped him; he dropped the gun, and all ran away. However, they recovered the gun and afterward killed a man. That case was probably in line with what Dr. Bender has discussed. The Negro boy was one of 19 children of one mother, and a twentieth was coming; 2 brothers were in institutions for the insane. One brother was definitely a criminal character and was at the Dannemora State Hospital, Warwick, N. Y., and another was at the New York State Training School for Boys. The older Italian boy was of a low moron type; the younger was normal (if there is a norm) so far as could be discovered, but it seemed to me at that time the younger brother identified himself with the older, whose deeds he wished to emulate.

I was particularly interested in Dr. Bender's discussion because not only I but nearly all my colleagues on the bench rely on her judgment and findings. It is personally gratifying to note that she has broken away from mere theorizing and has discarded—at least so I judge—the belief that statistics are controlling. In her consideration of the behavior problems of children in relation to their psychotic and criminal parents, she also notes that in the majority of cases behavior disturbances in children are due to reactions of the children to unfavorable home situations resulting from the loss either of the mother or the father, for one reason or another. This statement is substantiated to a great degree in the court. My colleagues and I find that behavior problems in children are generally due to disturbed home conditions, sometimes by reason of the loss of the mother and sometimes, probably often, because of difficulties that arise between the parents.

There are two important periods in the life of a child. Even I know that, though I am not a psychiatrist and so did not delve into the problem from a purely scientific angle. Children are brought into the court at the age of 8 or 9 years, and an attempt is made to fasten on them the stigma of delinquency. Most judges feel that one cannot find a child of 7, 8 or 9 years delinquent. Most of my colleagues and I find it hard to find a child of 15 or 16 years delinquent because we look into the causative factors that produce these delinquencies. The early period in the life of a child is the first of those which I should like to call the trait or character-forming periods; the other is the period of early puberty and, possibly, of the entire adolescence. At that time the child is most vulnerable; he is impressionable indeed. An unfavorable home life or parent-child relationship in early childhood or a little later, during the period of adolescence, tends, therefore, to mold the character and fix the type of conduct that the child will manifest.

My experience has taught me that children who appear to be defective are in fact not always so. Much stress has been laid on intelligence quotients. I do not know how much one can rely on them. I know that Dr. Bender and the court psychiatrist always give me the intelligence quotients of the children who are sent to them for psychologic tests. A child may have a low intelligence quotient and, at the same time, be possessed of rare possibilities. I have found that to be a fact in many instances, whereas, on the other hand, a child with a high intelligence quotient may, because of a neurosis, be a menace to himself and to society. A lad about 11 years of age who was brilliant had an intelligence quotient of 147.

He was the product of a broken home and gave definite indications not of asocial but of antisocial tendencies. I still have him with me; he is not only a menace to himself but a potential menace to the community. For instance, I placed him on parole in order to help him. I thought it wise to remove him from the sphere in which he had been functioning. I thought the mother, who was hypochondriacal, had a detrimental influence on the child, so it was a condition of the parole that he was to go to a relative, to be divorced from the home which had produced the delinquent tendencies. While on parole he was brought back to me for having snatched a pocket-book from a perambulator. The woman identified him as the child who had snatched the pocket-book. He was apprehended two blocks away. He had been seen leaving the hallway of a tenement house and running across the street. When taken into custody he did not have the pocket-book, in which the woman said that she had had about $25, nor did he have the money. The hallway of the tenement was searched and the pocket-book was found, but not the money. The boy denied absolutely having taken the pocket-book. It was my duty to decide whether or not he was guilty. I decided that he was and remanded him to the Children's Shelter of the New York Society for Prevention of Cruelty to Children, so that he might be studied psychiatrically and psychologically. I asked a probation officer to talk to him intimately. The child then disclosed that there was another boy. I asked that the other boy be brought to see me. He told the whole story. It was arranged that the one boy was to run into the hallway, take out the money and then run across the street and pass it to the other boy, who was standing on the other side of the street, so that he would not have the money found on him when caught. One can see what is the type of that boy. I think I am right, then, in saying that a high intelligence quotient does not always indicate normality.

Children must be approached in the light of their individual responses rather than on the basis of the results of general or standardized tests. I find that sometimes children show a lack of ability not because there is an inherent lack but because there is a tendency to force them to do that for which they have a natural dislike or for which they have no natural bent. Even in children of parents with inferior or neurotic personalities, or even with schizophrenia, there will result a more or less normal development.

It was my privilege to see Dr. Bender's paper before she read it. I was impressed with the idea, though not explicitly and specifically expressed, which runs through her paper: that individualization of the child is an important factor from the point of view of treatment or rehabilitation or of prevention of the development of antisocial attitudes. I have always feared institutionalization and still do. To me it means standardization. I think that if in the treatment of children one accepts standards without regard to the particular child the purpose of the treatment will be lost. Fortunately, the human being is not a standardized product. Life would be a bore if all were of one pattern. Everything possible should be done to prevent standardization. We in the court try to avoid this as far as it is within our capabilities. Even when we have to treat children, we wish them to be regarded as distinct human worlds and each case to be investigated and the proper approach made in the treatment of that particular human world.

DR. FLORENCE POWDERMAKER: Dr. Bender's contribution to the study of genetics presents a unique and dynamic picture, quite different from the usual statistical one, and it represents a valuable pioneer movement in the direction of a deeper understanding of familial influences. The work interests me particularly because of a recently finished summary of a study of 80 delinquent girls between the ages of 12 and 16 years. Twenty per cent of these girls had a parent with psychosis serious enough for institutionalization, and 24 per cent had a father who had been either a deserter or a chronic addict to the use of alcohol or who possessed a criminal record; no mothers were in the groups last-mentioned. Thus, approximately 40 per cent of the girls had had either a psychotic or a criminal parent and had themselves found their way into the Children's Court as delinquent

or neglected children. In the actual study of the children I found that the court charge as to delinquency or neglect is no indication of the actual behavior or of the importance of the psychologic problem.

An interesting point in Dr. Bender's paper was the distortion of the personality of the child when there is a parent with schizophrenia. She mentioned this occurrence particularly when the father had a paranoid type of schizophrenia and the child was a boy. I have found no less interesting results in girls when the mother had schizophrenia. The distortion of personality is marked, and in some cases in which I was able to analyze rather deeply I found that these distortions seemed to be related to the problem of identification and object relationship. Confusion results because the girl rejects her psychotic mother and identifies herself with the father, who is also the male love object. When situations arise in the Oedipus relation in which there is a great deal of guilt, the girl identifies herself with the mother, and more trouble develops. When a later situation arises in which there is insecurity or guilt, the tendency again is to identify herself with the psychotic mother.

An example of a problem of this type was shown in a girl whose mother was extremely unstable and whose father was a criminal, having been imprisoned twice for robbery. The girl was the favorite child of the father and was completely rejected by the mother. The mother identified the girl with the father, frequently telling her she was just like him. The girl had a long history of stealing and running away, and she tried to commit suicide. The father had frequently said in the girl's presence that he would rather die or be in jail than live with the mother. The girl had lived out his situation completely.

Another point in Dr. Bender's paper that interests me is the discussion of the so-called psychopathic children, particularly those who came from homes that offered little or no love and emotional security in their early years. I have found a similar group of children. They are hyperkinetic. They can have no real emotional relationship with any one. Although they may show a superficial affection, it does not amount to anything. They are impulsive and cannot be kept at regular tasks. There is a superficial kind of guilt but none of any depth. They show no anxiety. Therapy has failed with these children, even in a period as long as three years. Besides intensive psychotherapy, the best environmental therapy available, that is, placing them in small, free homes for girls and in private families, under careful supervision, has been tried. Hyperkinesis diminishes, and the children can be taught a certain amount of routine; more than that has not been accomplished. It has been my habit to call these girls not psychopathic but emotionally defective. They seem not so much pathologic as defective in the ability to fix affection on any person. All the children from their earliest history show that they have never had any emotional attachments. The parents have either deserted or have been psychotic. The children are unable to make emotional attachments later in life, and it seems to be a real defect in personality rather than a pathologic situation. Whether it is constitutional or not, one does not know. It seems to me that a continued study of this particular group may give interesting results for an understanding of the development of personality.

DR. LAURETTA BENDER: It is kind of Judge Panken to come here and discuss my paper. There has been a close relationship between the Children's Court and my service, particularly in the past year. At least half the children have been sent to us by Judge Panken and his colleagues.

The problem of individualization which Judge Panken emphasizes can best be solved by allowing the child to carry on a normal life, with a normal father and mother, in his early years. If this is impossible, one should try to obtain adequate substitutes immediately in a home environment.

PREPSYCHOTIC PERSONALITY OF THE PATIENT WITH ANXIOUS, AGITATED DEPRESSION. DR. WILLIAM B. TITLEY (by invitation).

This article will be published later.

NEW YORK NEUROLOGICAL SOCIETY AND NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY

Joint Meeting, May 12, 1936

LEON H. CORNWALL, M.D., *President, in the Chair*

SPASTIC PSEUDOSCLEROSIS, WITH A REPORT OF ITS OCCURRENCE IN THREE MEMBERS OF THE SAME FAMILY. DR. A. M. RABINER, Brooklyn.

The 3 patients whose cases are reported here are shown as a family group. The clinical picture presented is that produced by multiple lesions of the central nervous system. While in the individual case a diagnosis of multiple sclerosis could be made, this diagnosis is untenable for the entire group. The first case was studied pathologically by Dr. Charles Davison at the Montefiore Hospital and was reported by him as one of spastic pseudosclerosis (*Brain* **55**:247, 1932). At that time the presence of a similar affection in other members of the family was not suspected. I do not think that the term spastic pseudosclerosis applies to the condition in this family group. Numerous instances of familial syndromes simulating multiple sclerosis may be found in the literature. Neuropathologists describe many pathologic pictures which cannot be differentiated from that of multiple sclerosis; at times these follow infectious disease, but often there is no known etiologic agent. The condition in this family belongs in the latter category. In all 3 instances hypertonicity of one of the lower extremities appeared at the age of about 30 years. One must conclude that this type of disorder is based on a malformation of the central nervous system which gives rise to the first symptoms in adult life. Other familial groups in which there is no history of infection may be regarded as having a similar etiology.

CASE 1.—J. R. at the age of 29 years (1928) began to notice stiffness in the left knee. Thereafter the gait became awkward, and clumsiness in the use of the left arm appeared. Later, speech was altered and handwriting impaired. Six months later, at the Mount Sinai Hospital, he presented an attitude suggesting parkinsonism; there was generalized spasticity, especially on the left, with a tendency to a hemiplegic gait and a slight toe drop on the left. The Romberg sign was elicited. Clumsiness of both hands and feet, slow, expressionless speech and overactive deep reflexes, greater on the left than on the right, were noted; the abdominal reflexes were present. Adiadakokinesis, with marked asynergia, was more definite on the left. Weakness of the left side of the face, with deviation of the tongue to the left, was noted. The left leg was weak. An equivocal Babinski toe sign was elicited bilaterally. The visual fields and spinal fluid were normal; the Wassermann and other laboratory tests gave negative results. The diagnosis rested between multiple sclerosis and a postencephalitic syndrome.

One year later, at the New York Neurological Institute, the diagnosis of multiple sclerosis was made.

The patient was admitted to the Montefiore Hospital at the age of 32 (May 1930). Examination revealed aphonia, involuntary movements of all limbs, generalized muscular atrophy with fibrillations and increased muscular tonus and diminished power in all limbs, with bilateral pyramidal tract signs. Sensation was intact. The right corner of the mouth drooped; there were almost ceaseless forced laughter and crying and oily facies, with the mouth constantly half open in a manner reminiscent of Wilson's disease. Electrical tests revealed normal results. Laboratory tests showed nothing abnormal. Death occurred in November 1930.

CASE 2.—D. R., aged 39, married, with 3 normal children, a sister of J. R., was admitted to the Beth Moses Hospital, Brooklyn, in December 1935. Four months prior to examination she first noticed stiffness of the right leg. This had become worse. More recently, she complained of frequent attacks of dizziness

and had fallen on three occasions, the last time sustaining extensive bruises of the face. There was no loss of consciousness in any of these attacks. She had not suffered from headache, nausea or vomiting.

Examination revealed ptosis of the left upper lid, central facial weakness on the right and bilateral atrophy of the temporal and masseter muscles. The ocular fundi were normal. In walking the patient swayed from side to side, dragging the right leg. The right foot was dropped and inverted. The tendon reflexes were all overactive; there were ankle clonus on the right and bilateral Oppenheim and Rossolimo signs; the Babinski toe sign was not obtained. The abdominal reflexes were not elicited. There was ataxia in the finger to nose and heel to knee tests; sensory examination gave negative results. The facies presented a peculiar fixity of expression. Routine serologic tests of the blood and spinal fluid gave negative reactions, as did the icteric index, van den Bergh, galactose tolerance and bromsulphalein tests and the blood chemistry determinations.

The patient has been examined repeatedly since December 1935, the last occasion being on March 25, 1936. There has been practically no change in the status, except that she seldom walks without aid, because of the fear of falling.

Case 3.—S. R., aged 35, married, a musician, a brother of J. R., who was admitted to the Kings County Hospital, Brooklyn, on Dec. 2, 1935, gave a history of weakness of the right foot of eight months' duration. The onset had been gradual for two months; then he began to drag the leg. No pain or other complaint was noted, except occasional dizzy spells in the two months prior to examination.

Examination revealed normal ocular fundi, except for a congenital epipapillary membrane overlying the right nerve head. The right pupil was larger than the left. There were a few horizontal nystagmoid oscillations on lateral gaze. The right lower limb was weak; there were a foot drop on the right, spasticity of the right leg and scraping of the right foot in walking. Coarse fibrillations were observed in the muscles of the right thigh and calf. A slight intention tremor was seen in the finger to nose test. There was a Hoffmann sign on the left. All tendon reflexes were overactive, more so on the right, with an equivocal Babinski toe sign on the right, Rossolimo sign on the right and a positive Mendel-Bechterew sign bilaterally. The abdominal reflexes were present. Sensory examination gave normal results. Routine laboratory examinations of the blood and spinal fluid, including chemical studies, gave normal results.

The patient was reexamined on March 22, 1936. The status was unchanged. He is working regularly.

DISCUSSION

Dr. Charles Davison: Dr. Rabiner's cases conform in some respects to the case which I described. The similarity includes involvement of the pyramidal tracts, slight cerebellar signs and atrophy of muscles. Neither of the 2 patients in this family, if I am correct, have presented mental symptoms or extrapyramidal system signs. I wonder whether, in the absence of the mental symptoms and extrapyramidal signs, one is justified in calling the condition in these cases spastic pseudosclerosis. In the true sense it is not pseudosclerosis. Becaue of the extrapyramidal signs and the spasticity, Jacob called the disease spastic pseudosclerosis. Clinically and pathologically, I think these cases are far from being instances of true pseudosclerosis. In none of the cases reported in the literature were the extreme rigidity and tremor shown that one is accustomed to see in Wilson's disease or pseudosclerosis. There is no question that the two diseases differ histopathologically, for in none of the cases of spastic pseudosclerosis was there observed cirrhosis of the liver or Alzheimer glia cells. In the case I described Alzheimer glia cells and cirrhosis of the liver were also absent. At that time, because of the diffuse process in the cortex, extrapyramidal symptoms and disease of the anterior horn cells, I suggested the term encephalomyopathy. I wonder whether, except for the scanty cerebellar signs, Dr. Rabiner's 2 cases do not fall into the group of amyotrophic lateral sclerosis. If the cerebellar signs are eliminated there remains a typical upper and lower motor neuron syndrome,

which is typical of amyotrophic lateral sclerosis. As in Huntington's chorea and other hereditary neural disorders, there is the possibility that the inherited disease may assume a different form. This also applies to the family described by Dr. Rabiner; one or several members may have amyotrophic lateral sclerosis, and others, as the member I described, may suffer from spastic pseudosclerosis. As a fact, in the case I described the condition was at one time considered to be amyotrophic lateral sclerosis, with mental symptoms.

DR. FRANK J. CURRAN: I wish to ask Dr. Rabiner if an examination was made for a Kayser-Fleischer ring. In cases of pseudosclerosis this has always been regarded as a diagnostic feature.

DR. A. M. RABINER: The woman I described has mental symptoms. She is euphoric, emotional and apprehensive about her illness. She refuses to leave the house now.

As regards extrapyramidal symptoms, the drop foot in both cases represents, I think, definite striatal involvement. The foot is rigid and hypertonic. In neither of my cases has there been a true Babinski toe sign. The musculature of the foot varies in tonicity. Certainly, one is justified in considering that a foot of that type indicates extrapyramidal involvement—a striatal lesion.

I did not use the term encephalomyopathy, for I still do not know what myopathy or encephalopathy means. To me these terms are a sort of waste-basket, and that is why I avoided them.

I wish to emphasize that in each of the 3 cases the disease began in the same way, with rigidity or spasticity and foot drop. Dr. Davison's patient had the most advanced stage. The first case in the series appears next in respect to the severity of involvement, and in the third case there was only disability of the right leg. All the patients presented fibrillations, but I do not think amyotrophic lateral sclerosis would explain the definite cerebellar signs.

There was no Kayser-Fleischer ring in these cases, though it was looked for. Both patients were studied thoroughly for evidences of disturbance of liver function. All tests gave normal results.

ROENTGEN THERAPY IN CASES OF ENCEPHALITIS. DR. SAMUEL A. GOLDBERG, Newark, N. J. (by invitation).

On the basis of the hypothesis that some of the symptoms in encephalitis are due to lymphocytic mantling in the perivascular spaces and the observation that lymphocytes are known to be highly sensitive to roentgen rays, it was thought that small doses of these rays applied to the lateral aspects of the head might be beneficial in the acute stage of the disease.

In an experimental trial mice were inoculated intranasally with the St. Louis strain of encephalitis virus and were given ten or twelve daily treatments of five minutes each; 42 per cent of the mice survived. Of the mice given only five daily treatments of two minutes each, 27 per cent survived. Of an equal number of control animals which were inoculated at the same time but were not treated, all but 1 died.

Clinically roentgen treatment of patients with fully developed postencephalitic parkinsonism gave negative results. Seventeen patients in the acute stage of encephalitis were treated with small doses of roentgen rays. The results were consistently satisfactory. While the optimum dose has not been determined, the best results have thus far been obtained with the following set-up: 135 kilovolts and 5 milliamperes, given at a distance of 15 inches (38.1 cm.), with a 3 mm. filter of aluminum for two minutes with no cone, a dose which is equal approximately to 40 roentgen units. This dose is applied alternately to the lateral aspects of the head at intervals of forty-eight hours in a series of ten or twelve treatments.

It is thought that in the treatment of encephalitis the roentgen rays may act by relieving the pressure on the brain tissue next the perivascular lymphocytic collars, by lessening the obstruction to the circulation or by dissolving the lymphocytes so that an added amount of enzyme or antibody capable of destroying the

virus may be liberated. Irradiation of the St. Louis strain of the encephalitis virus in vitro with doses equal to three times the total exposure used for the patients did not alter its virulence for mice.

The treatments should be instituted as early as possible to prevent permanent damage to the nerve tissue.

From the results obtained experimentally and clinically it seems that roentgen therapy in the acute stage of encephalitis is worthy of trial.

DISCUSSION

DR. E. D. FRIEDMAN: It is difficult for me to discuss this paper, for I cannot speak from personal experience with this treatment for acute encephalitis. My experience with it even in cases of chronic epidemic encephalitis has been meager. I have seen 2 or 3 instances of chronic encephalitic parkinsonism in which the disease was treated with this method, without any striking change for the better, and I believe that Marburg and Sgalitzer (Marburg, O., and Sgalitzer, M.: Röntgen Behandlung der Nervenkrankheiten, in Bumke, O., and Foerster, O.: Handbuch der Neurologie, Berlin, Julius Springer, 1936, vol. 8), who did pioneer work in this field, came to the conclusion that the prospects for relief with this method of treatment for chronic encephalitis are not good.

It is generally conceded, as Dr. Goldberg has said, that the roentgen rays have a destructive effect on lymphocytes. I need only recall the ease with which the enlargement of the glands in various forms of lymphadenopathy, including Hodgkin's disease, can be made to recede with roentgen treatment. There is also another effect of the roentgen rays, namely, that on the blood vessels. The capillaries particularly are vulnerable; the endothelial cells lining the capillaries become altered, so that the permeability of the wall is increased. Under such circumstances one would expect an increase in the edema as a result of roentgen treatment. However, the observations made by Dr. Goldberg seem, to him at least, to indicate the opposite effect.

I wonder also whether the whole story is told when one assumes that the symptoms are due to perivascular cuffing. After all, the perivascular cuffing is merely an expression of tissue reaction to a virus which is not sufficiently chemotactic, shall I say, to bring out a granulocytic response; one encounters a similar lymphocytic reaction in tuberculosis and in syphilis. By the same token, one would expect benefit from high voltage roentgen therapy in these conditions as well. I doubt whether there is sufficient constriction of the walls of the vessels in such cases to produce actual anoxemia of the tissues, with resulting impairment of function. That I, for one, cannot conceive. Of course, this discussion is entirely theoretical. Dr. Goldberg's experience may be of more value than my theorizing.

It is generally conceded that roentgen rays have a better effect on so-called infiltrating lesions than on productive glial reactions. Since it is known that in every case of encephalitis there is considerable glial response, I wonder whether the symptoms which develop on the basis of encephalitic virus infection are not due as much to glial proliferation as to cellular perivascular cuffing.

May I say further that most neurologists would not agree with Dr. Goldberg's statement that the diagnosis of epidemic encephalitis cannot be made unless one demonstrates changes in the spinal fluid or sees full-fledged parkinsonism? Many neurologists have undertaken to make the diagnosis purely on clinical grounds—on the basis of a group of symptoms which indicate multiplicity of lesions in the nervous system and which follow or are coincident with the acute infection.

From Dr. Goldberg's thesis one must conclude that the effect of irradiation is not on the virus itself; I do not understand to what the beneficial effect of this method of therapy is due. Besides, I wish to remind him that in many cases parkinsonism does not develop within a brief period after the initial infection; it will therefore be important for him to watch his patients for six, eight or ten years before he can state with any degree of certainty that there will not be late encephalitic sequelae.

DR. C. W. SCHWARTZ: Roentgen irradiation is undoubtedly of benefit in many forms of acute infection. Its efficacy in the treatment of carbuncles and furunculosis is well known, and its favorable influence on cellulitis, erysipelas, infectious granulomas and parotitis has been known for some time; this year the whole subject has been reviewed and amplified by Hodges (*Am. J. Roentgenol.* **35**:145, 1936).

The question which is always asked regarding any form of therapy is: What is the modus operandi? Why does it work? Manges, in a recent editorial (*Am. J. Roentgenol.* **35**:399, 1936) in which he commented on this form of therapy, recalled that quinine was as efficacious in treating malaria before as after the discovery of the plasmodium. With the roentgen rays one is now in a similar prediscovery period. It works, but on what it is not known exactly. As Dr. Goldberg has pointed out, the lymphocytes and leukocytes are highly sensitive to roentgen rays and disintegrate rapidly under the action of relatively little radiation. This probably liberates whatever chemical they contain which has a strongly bactericidal action. I see no reason to believe that such small doses have any appreciable effect on either virus or bacteria, both of which are about as resistant to roentgen rays as the average body tissue. I believe strongly that the action of radiation therapy is an effect not primarily on the structure of the cells themselves but on the chemical cellular environment. The ionization produced by roentgen rays has a tendency to flocculate positively charged colloids, and proteins are probably colloid systems, for they are composed of large polypeptid molecules; roentgen rays also raise somewhat the hydrogen ion concentration, which in turn may activate dormant enzymes; these may bring about the apparent autolysis of the so-called roentgen sensitive lymphocytes and leukocytes and so destroy the offending virus.

Of course, as Dr. Goldberg has pointed out, this form of therapy has little to offer in the chronic stage. My colleagues and I have proved that to our satisfaction at the New York Neurological Institute. However, I have been of the opinion for some time that there is something to be offered in the acute stage which may eliminate, or at least minimize, the usual sequelae, and I believe that Dr. Goldberg has done a real service in bringing this subject to the attention.

DR. LEON H. CORNWALL: I have read two of Dr. Goldberg's published papers, in addition to hearing his presentation this evening. I am impressed by the evidence which he has offered. It seems to me that his work demands serious consideration and further investigation of the effects of roentgen rays in the treatment for lethargic encephalitis. I doubt whether many neurologists will agree with his hypothesis that the symptoms are caused by the perivascular exudate and by circulatory changes. Certainly, no neuropathologist will. The rôle of circulatory changes is difficult to disprove, and it is not possible to disprove that lymphocytic infiltration may exert pressure. There are, however, so many other features in the lesions of encephalitis that I can scarcely conceive of removal of perivascular cuffing as being the reason for the favorable results. The neuropathologist would consider that the cellular exudate is merely a manifestation of an inflammatory reaction, as Dr. Friedman has mentioned.

These criticisms are merely minor, and they do not impair in any sense the value of what Dr. Goldberg has done.

DR. S. A. GOLDBERG: I did not mean to state that all symptoms are due to perivascular mantling and pressure. If I had had more time I should have shown slides demonstrating some of the pathologic changes. At the beginning of fibrosis, of course, lymphocytes play an important rôle. This stage is preceded by lymphocytic infiltration so that gliosis and fibrosis are not present to any degree in the acute stage of the disease. My original hypothesis may be wrong. It was on that basis that roentgen therapy was deemed suitable, but the exact action of roentgen rays is not definitely known.

What the ultimate condition of these patients will be I do not know, and I am also aware that many years may pass before the postencephalitic parkinsonian syndrome develops.

VALUE OF PSYCHOANALYSIS AS A THERAPEUTIC PROCEDURE. DR. HAROLD THOMAS HYMAN.

The literature of psychoanalysis contains few tangible data concerning its value as a therapeutic measure. The economic structure of psychoanalysis has given rise to great distrust among practitioners. It is estimated that the average analysis costs approximately from $5,000 to $6,000 before it is terminated. Medical limitations to analytic therapy have not been defined. So far as can be ascertained, analysts confess to no failures and believe that their therapy is applicable to the whole human race and all its psychiatric ills.

This communication is concerned with an analysis of the cases of 43 patients who were analyzed in the past sixteen years. All were referred by me and my late colleague (Dr. Leo Kessel) to leading psychoanalysts. Fifteen of the patients suffered from profound psychiatric diseases, 6 from manic-depressive psychoses, 5 from schizophrenia, 2 from homosexuality, 1 from constitutional inferiority and 1 from chronic addiction to alcohol. In this group there were 12 failures in treatment. In 2 instances the analysis was incomplete, and the results were questionable. In 1 case of homosexuality a brilliant cure was effected. The remaining 28 patients suffered from less ominous neuropsychiatric symptoms. This group included patients with hysteria, anxiety states, anxiety hysteria, mild depression, phobias and obsessions, impotence and frigidity, behavior problems, hypochondriasis, and, in at least 1 instance, psychosomatic abnormality. Four patients experienced remarkable cures. Another group of 13 patients were distinctly benefited by therapy, but in these instances altered conditions of life also contributed to the successful result. Eleven of the last-mentioned group of 28 patients experienced no benefit. This group included 1 patient with impotence, 1 with frigidity, 3 with hypochondriasis, 5 with anxiety neuroses and 1 with an unclassifiable syndrome.

It is my belief that psychoanalysts owe a definite statement to the medical profession concerning their limitations. I believe that the present therapy is limited to persons who can afford from $5,000 to $6,000 for treatment, that it is best suited to the minor disorders and not to the severe psychiatric abnormalities and that the limitations should be further drawn by confining therapy to patients in this group who are between the ages of 25 and 45 and have had some type of professional or artistic training, so that they are able to grasp the importance of the therapy that is offered them.

DISCUSSION

DR. BERNARD SACHS: I wish to consider this subject seriously. It is fortunate that there has been presented the point of view of a general practitioner of wide experience, or of two men with such qualifications, as Dr. Kessel was intimately associated with this investigation. The discussion will have little to do with the acceptance or nonacceptance of the freudian doctrine. I have stated on many occasions why, even to this day, I cannot accept the general conclusions of the freudian doctrines. Too much is simply assumed; little is proved, and throughout there is such an utter lack of logical deduction that any man who has been trained to think logically cannot accept the doctrines, unless it is claimed that they are articles of faith and nothing else—and with articles of faith I am the last to quarrel. But the doctrines are not the subject of discussion. I want only to say that I am sure some who read as much of present day psychoanalytic literature as I do must have been startled by the fact that Dr. Brill has now conceded that some of the doctrines of Freud are of hippocratic origin. In a learned article Dr. Brill has admitted that these doctrines are not so novel as they are supposed to be and that what is good in them has, to a large extent, been anticipated by others. Some things, I grant, are peculiar to the school, particularly the instance which was referred to in this paper. Hippocrates referred to sex, but he did not say sex was everything—far from it.

Dr. Jelliffe said in a recent article that the psychiatrist is a "born trouble hunter." I think that is about as good a definition of a psychiatrist as any I have read. He is a trouble hunter, and he will go deep in order to find trouble if it is

not on the surface. That leads to the one serious objection I have to the theory in its application to practice. I shall not take up the financial side. I do not care to do that, though I think there is much justice in Dr. Hyman's statements. My chief objection—and I say this deliberately and am willing to stand by every word—my chief objection to the application of the psychoanalytic doctrine is that it is a disruptive and not a constructive mechanism; I use the term disruptive rather than the word Peterson employed (Peterson, Frederick: Creative Re-education, New York, G. P. Putnam's Sons, 1936, p. 99); he called it a destructive process. If it is not destructive, it is at least disruptive, and my objection to the application of this method is that, instead of curing mental disease, it more often prolongs and engenders it. I am astonished by the frankness of acknowledgment on the part of the more conservative psychoanalysts that, while they can cure the neuroses, they are careful about claiming that they can cure the psychoses; yet in one institution after another patients suffering from various forms of insanity, especially manic-depressive psychoses and dementia praecox, are treated for years; a burrowing goes on in their minds which often makes them worse than when they entered the institution. I charge the psychoanalysts with this: They engender mental disease rather than cure it; any one can bring proofs in cases in which patients who have been subjected to the psychoanalytic process have become more introverted and more hypochondriac than they were and their mental disease, instead of having been lessened by this wonderful method of "free association," which is not free association at all, has become intensified. I am so convinced of this that I begin to doubt whether any person who has been psychoanalyzed is ever entirely normal mentally thereafter. There is more truth in this than may appear at first.

I have no objection to the psychoanalysis of adults; I say, let the psychoanalyst go as far as he pleases, or as far as the patient will let him. But I want him to keep his hands off children. In children up to the ages of 12, 15 and 16 years the amount of damage that is done is outrageous. I consider the psychoanalytic method in the examination of children a perilous form of therapy, and I can point to any number of children who have been made miserable or insane rather than cured of any early psychotic or neurotic symptoms that they may have had. It is good that a man like Dr. Hyman should tell of the failures in psychoanalysis. I think he has given as roseate a picture as possible. His analysis of the statistics has been a little more favorable than mine would have been, but I am trying to say this: The psychoanalysts have claimed too much, and for that reason it is well that this subject should be brought up for discussion. I hope that some day the psychoanalysts will come before this society and explain the actual basis for the acceptance of the Oedipus complex. All assume it and talk of it, but how much is there in the claim that the Oedipus complex plays any rôle? Freud himself said that it does not apply to normal persons; yet the psychoanalysts are always talking about the Oedipus complex, so that every one believes it is almost gospel truth. Then the infantilists are always talking about infantile sexuality. Let them stand up and give positive evidence, if they can, that that is the cause of mental and other disturbances which occur at the age of 25 or 30 years. I want the exact proof. I have great respect for Freud's genius, and, as you know, I have a personal respect and friendship for him. It is all well and good to admire genius. At the same time, when we, as scientific men, are asked to accept doctrines, we have a right to demand proof. The question of infantile sexuality needs further proof, and while I am willing to acknowledge that perhaps a few things have been learned regarding the subconscious, I think that there is not always the absolute evidence for the part it plays that is attributed to it. For example, the Supreme Court has decided that a man is responsible for his conscious acts; the subconscious does not play any part in the public courts.

I want to add that there is nothing personal in this controversy of mine, as far as my feelings toward any of my colleagues are concerned or as regards the number of patients who go to the analysts. I have always been interested in the individual patient, but at this time of my life I am more interested in the citizen

than in the patient; for that reason, I feel so strongly about the disruptive influence of psychoanalysis, for it is not helping to educate; rather, the psychoanalysts fail to educate a decent citizenry through their influence particularly over young mothers, who are captivated by talk about sex. Who would not be? The aberrations and importance of sex have been introduced into the minds of young mothers to such an extent that they have neglected other far more important duties. I see lists of parent-teacher associations, child study associations and similar organizations given over to talks on sex. Recently one of them published a volume of articles on sex education contributed entirely by women; so, in a short reference to this book, which some may read in a few months, I said I should like, as a mere man, to tell the women that the men also have something to do with the question of sex and sex education. So much stress has been laid on the question of sex and it has been overemphasized to such a horrible extent that children are not trained to be truthful, honest, kind, just and liberty loving. The "trouble hunter," as Dr. Jelliffe calls the psychoanalyst, goes muck-raking after minor sexual sins of commission or omission, I do not know which. These are some of the reasons that I think the psychoanalytic doctrine is a pernicious doctrine, so far as public morality and public decency are concerned. With that I need say nothing more.

DR. LAWRENCE S. KUBIE: There is, in reality, no such thing as "the therapeutic value of psychoanalysis," any more than the therapeutic value of surgical or medical treatment. The efficacy of surgical intervention in appendicitis is not the same as that in tumor of the brain; a brain tumor differs from a brain abscess and a brain abscess from a bony tumor, and even an appendix does not show the same therapeutic responses when it is acutely as when it is chronically inflamed or already ruptured. To speak of the therapeutic efficacy of surgical treatment is, therefore, impossible, and in the same way, it is impossible to speak of the therapeutic efficacy of psychoanalysis. One must discuss it in terms of specific neuroses, and of these neuroses at various stages and under favorable and unfavorable life situations. To do this necessitates a large and difficult survey, which can be made only over many years. Therefore, though I might be glad to hear of Dr. Hyman's experience, I cannot use it as a guide to the therapeutic efficacy of psychoanalysis from a truly scientific standpoint.

Dr. Hyman reported a group of 43 cases, of which 33 were included in a previous report (Kessel, Leo, and Hyman, Harold Thomas: The Value of Psychoanalysis as a Therapeutic Procedure, J. A. M. A. **101**:1612 [Nov. 18] 1933) and 10 are added here. In their wide variety they form a cross-section of psychoanalytic practice, but this very fact limits their usefulness for statistical survey. One might also cavil at the inclusion of outspoken perversion among the psychotic patients in the group with "grave psychiatric disorders," since perversion presents such different technical and internal problems. One can have no quarrel with Dr. Hyman's emphasis on the importance of being thoroughly frank with the patient's family when one is dealing with persons with psychoses, nor with his insistence that with this group of patients any therapeutic venture in analysis must be undertaken on an experimental basis.

When it comes to the question of analytic therapy for psychoneuroses in general, Dr. Hyman recommends first a period of trial, with efforts at superficial readjustments. This recommendation is superfluous; such efforts will always be made first, with greater or less intelligence. Some psychiatrists and some general practitioners have a genius for helping patients to adjust their lives within the limits of their neuroses. The effort of psychoanalysis, however, is to destroy the neurosis itself. Sometimes this achieves a far greater victory. Sometimes the effort not only fails but may be disturbing. It is a matter of nice psychiatric and psychoanalytic judgment to determine when it is wise to attempt the more fundamental form of treatment and when to rest content with the effort to help the patient to adjust his life within the limits of an uncured, untreated neurosis. One might, therefore, suggest to Dr. Hyman that in reaching this decision the judgment of an analyst should also be taken into consideration. An experienced analyst is not eager to leap in where the odds are too heavily weighted against him.

Dr. Hyman's record of 17 of 28 patients in this group who were distinctly benefited is encouraging, even with the sound qualifications and reservations with which he limits his enthusiasm. In my experience, however, I do not believe that patients in late adolescence and the early twenties are inaccessible to successful analytic help. I have seen extraordinarily valuable preventive results accomplished in this period, early hypochondriac and hysterical depressions that seemed headed toward definite schizophrenic development swung back into full normality, early manifestations of homosexuality aborted, homosexual panic states of the pre-paranoid variety cured, fully developed states of invalidism relieved, etc. It is a period which presents certain distinct technical difficulties, but I do not believe that these are insurmountable in either sex.

Here, I wish to point out a few things which must be known in a case in order to evaluate the course and outcome of an analysis. In my recent book (Kubie, Lawrence S.: Practical Aspects of Psychoanalysis, New York, W. W. Norton & Company, 1936), I claimed that even of the layman one has the right to demand that he know these five fundamental facts before attempting to pass judgment: (1) whether the patient was analyzed by a competent analyst for an adequate length of time; (2) the symptoms and difficulties which brought the patient to the analyst for treatment and the normal outcome of such a condition if it were not treated; (3) the usual course and outcome of such a condition if the patient were analyzed under favorable circumstances; (4) specially favorable or unfavorable influences which affected the progress in the particular case, and (5) the condition of the patient at the end of the treatment as compared with his condition in the beginning. This, however, is less than physicians ought to know, but it is distressing to see how rarely such knowledge is at the hand of persons who venture to pass judgment. In this discussion, however, one has an even graver responsibility, for one is trying to decide not merely whether an individual patient was benefited but what is the value of the procedure as such. I shall indicate briefly a few of the facts which must be known about every analyzed patient in attempting to build up a statistical gage of the value of psychoanalytic therapy: (1) The initial diagnosis, with the evidence for the diagnosis; (2) the general psychic state of the patient's life at the onset of the analysis, i. e., the extent to which the neurosis had already crippled the patient's life; (3) the general life situation of the patient at the onset of the analysis (economic, familial, marital and professional); (4) the conditions under which the analysis was undertaken (arrangements as to finances, time and travel); (5) the extent to which these conditions were adhered to throughout the analysis; (6) special difficulties against which the analysis had to labor and which arose from forces uncontrollable by the analysis (e. g., outside interference, physical illness and interruptions); (7) special advantageous circumstances which may have arisen and favorably affected the course and outcome of the analysis; (8) the duration and general course of the analysis; (9) the therapeutic outcome as estimated by (*a*) the final symptomatic state and (*b*) the final state of the patient's general life situation and his way of living, as compared with the conditions designated in items (1) (2) and (3); (10) the final diagnosis, based on the additional material uncovered in the analysis, and (11) the follow up observations.

Dr. Hyman deplores the absence of detailed or statistical studies of the results of psychoanalytic therapy. In this every one who is interested in the future of psychoanalysis must agree with him. It does not mean, however, as he infers, that there have been no efforts to achieve such information. The Berlin Psychoanalytic Institute attempted a survey of ten years' work, and these results have been published; because they fail, however, to give adequate data, such as I have outlined, they are not illuminating. More recently, Dr. A. Glover, the scientific director of the Institute of Psycho-Analysis (London) has begun the compilation of data through a careful questionnaire. The outcome of this investigation, when it is published, will be a step toward filling the gap to which Dr. Hyman refers.

Dr. Hyman levels the serious criticism at psychoanalysis that student physicians are charged for their training analyses. He calls this a violation of the hippocratic

oath. I do not believe that this charge is justified. A physician who is being trained in a specialty other than psychoanalysis often has to pay fees in post-graduate schools. If he goes abroad he pays fees to the hospital or to the clinic where he works, and if he receives individual instruction from a recognized leader in some specialty he pays that teacher for the instruction which he receives. It is true that in hospitals when, in the company of a group of students, he follows a physician on ward rounds or watches a surgeon in the operating room the fee that is charged is small and may be paid to the institution and not to the instructor. But it is an accepted practice that when the instructor gives a substantial amount of individual tutoring he looks on that as one of his means of livelihood and that such individual instruction should be paid for. In the organization of psychoanalytic training all theoretical lectures and seminars are carried on for the student's benefit at less than cost. The students pay low fees to the institution commensurate with those which they pay in any other training center. Nor are the teachers who instruct them paid for their services. Only at two points is payment involved—in the individual training of a candidate through what is called the training analysis and, later, in the sessions of the supervised individual clinical work. This is comparable to any system of individual instruction and is something that can hardly be looked on as outside general medical experience. When one man pledges himself to devote an hour of his time, day after day for months or even for two or three years, to the training of another man it is obvious that he is entitled to reasonable compensation for his services as personal guide, therapeutist and tutor.

Furthermore, it is important that the conduct of such instructional and preparatory analyses should be in the hands only of men of thorough training and experience. This limits the number who are available to do such work. If there were, let me say, ten recognized instructors of this order in a community, each carrying on two such preparatory training analyses, each analysis lasting for about two years, it is evident that only ten new trainees could be launched each year. Some of these might be in a position to pay moderate fees, and others, little. Clearly, there will always be a group of worthy expectant and eager applicants for training who must wait until, in the course of years, the number of thoroughly adequate instructors has increased enough to fill the needs of the community. Time itself is an essential factor in this growth of experience; there can, therefore, be no quick solution of this problem. The existence of a small endowment fund, which would help defray the expense of the preparatory analysis for worthy but indigent students, would ease the situation but would not eliminate the fundamental problem.

Similar considerations apply to Dr. Hyman's discussion of the economics of psychoanalysis. For instance, many analysts deplore the fact that psychoanalysis developed as a therapeutic instrument in private practice before it received widespread testing in nonremunerative medicine, where the objective impartiality of the analysts would not be constantly suspected. But I have never heard any one who understood the problem, whether he was friend or foe of analysis, contend that psychoanalysis could have had its inception in hospital practice. All know that the idea that the neurosis is a luxury of the rich is a fantasy without any basis in truth. All know, however, that the poor man's neurosis is not only just as severe as that of his wealthier neighbor but more obstinate, for, in addition to the essential tenacity of the neurotic mechanisms, life itself offers little incentive to him to seek health. Psychotherapy, whether it is analytic or otherwise, therefore tackles in the outpatient departments of the hospitals exactly the same internal psychic difficulties as those which are at work in the patients whom one sees in one's office, and it attempts to treat them under disadvantageous circumstances, with the dice loaded against it. In all dealing with psychoneuroses the discouraging internal forces are often so overwhelming that when, in addition, the external world fights against one's efforts human spirit has not the patience nor the courage to attempt to climb that impossible hill. This is one reason, among others, that I believe that the spread of psychotherapeutic influences into the lives of the masses will

not be fully achieved until the economic problem of poverty and destitution is solved or until such basic changes have been achieved in the methods of bringing up children that neuroses will be prevented rather than cured.

This may seem to be irrelevant to Dr. Hyman's challenge. I believe, however, that it touches the basic problem behind his arraignment. If I am right, it was unavoidable that analysis should develop first as a field of private practice. This was unavoidable but unfortunate, for it brought in its wake certain definite abuses. There is no use in denying that psychoanalysis has often been economically exploited. Eminent exponents have even corrupted and compromised with its fundamental technical principles for the sake of greater economic gain. The only method of combating this is through the education of colleagues in the medical profession, so that they will learn the difference between honest and dishonest analytic procedure, and the subsequent spread of that understanding to the laity. Ultimately, an intelligent laity is indispensable to the practice of intelligent and honest medicine, whether it is in the field of psychoanalytic medicine or elsewhere. I believe that what Dr. Hyman protests against are the abuses and not the inherent nature of analytic practice. With the protest against abuses I am in complete accord, but I wish to make clear the distinction between the abuses and the other problems which are inevitable under the present social organization. Dr. Hyman underestimates greatly the amount of generosity which analysts show in their dealings with patients. I have personally in the last two years been able to place nearly 17 patients with various experienced analysts, at fees ranging from $5 an hour to nothing. I have known analysts to pay for the analyses of patients in whom they were interested and whom they could not place. I have seen patients who started to pay an average fee and were then carried for a year and a half for nothing when their funds unexpectedly gave out. All this is to the credit of this much maligned group of analytic practitioners. I do not doubt, however, that any physician who has been in practice for any length of time could match this experience with others less pleasing. Whether analysts are more or less guilty in this matter than other specialists is hard to say and futile to speculate about.

It is worth stressing, however, that the analyst is in a peculiarly vulnerable position economically. He is the only specialist who has had to spend many extra years in preparation, whose economic security then depends on a small group of patients and whose income, therefore, is subject to extremely marked fluctuations. If he is not one of those who attempt to exploit this profession, he lives fairly close to the borderline of the balanced budget. When he undertakes the training of a colleague for a small fee or for nothing or when he undertakes the treatment of a patient under similar circumstances, he is committing himself not for an hour's operation, with a few hours of after-care, not for a consultation, with a few hours of consideration of laboratory and other reports, but for one, two or three years of his time, and this is a solemn commitment, which cannot be undertaken lightly.

In conclusion, I wish to say only that Dr. Hyman in his frank, and sometimes irascible, criticism is an invaluable friend. I keep hammering away, however, on the necessity of making a distinction between the essentials of psychoanalytic procedure and the abuses which are products of human frailty, for an instrument is, after all, only as valuable as the integrity of the persons who use it; this is nowhere more true than in the practice of analysis. I wish to emphasize, however, that there are many special features in analytic practice which put the analyst under a special strain and burden. That he has sometimes fallen is, unfortunately, true, but this should not obscure the fact that he has also conducted a steady struggle toward higher standards of training and of practice, a struggle which is in harmony with the best traditions of medical ethics.

DR. ISRAEL S. WECHSLER: It seems to me that the discussion has strayed rather far afield from the title of the paper. As it is, the title is somewhat contentious; it deals with personalities and centers on the persons who practice rather than on the procedure itself. Perhaps the title would have been better if

it had been "The Therapeutic Value of Psychoanalysis." As the other speakers have devoted themselves to generalities, I shall leave out controversies and limit myself to two points. So far, the discussion has been taken up by a pure internist, a pure neurologist and a pure psychoanalyst; I shall speak as a somewhat "impure" neurologist and psychiatrist, who occasionally "bootlegs" a little psychoanalysis. Of the two points to which I shall refer, one has repeatedly been pointed out, but nobody seems to pay attention to it; the other, I think, is even more important.

Psychoanalysis, it is well known, consists of three phases, not one. First, it is a body of psychology. It is not a doctrine; doctrines have nothing to do with psychologic concepts. Second, psychoanalysis is a method of investigation of the normal and abnormal workings of the mind. Third, psychoanalysis is a therapeutic procedure. Now, one may quarrel with the body of psychology; one may refuse to accept some or all of its postulates; one may quarrel with the numerous terms and, particularly, the concepts, such as the id, the ego and the superego, and one may take issue with the existence of the Oedipus situation or refuse to accept symbolism. One may quarrel even with the conception of the unconscious, although it is difficult to see how one can speak of psychopathology at all unless one accepts the Freudian concept of the unconscious. Once it is accepted, a number of other concepts, such as repression, regression and transference, naturally follow. One may, without violence to one's prejudices, accept the concept of sexuality, which certainly does not appear all at once at puberty. I imagine one can discard much of the theoretical side of psychoanalysis and still practice it.

The second point, namely, that psychoanalysis is a method of investigation, is perhaps the most important aspect of the problem. It is undoubtedly the best method vouchsafed in the last thirty or forty years. It has given more insight into mental problems than the method of introspection, observation of behavior or other psychologic methods which have to do with conscious processes. As a method, it can be dissociated from the body of analytic psychology, on the one hand, and the method of therapy, on the other. The important point is that psychoanalysis may be bad psychology and good therapy or bad therapy and good psychology. From this it follows that if one proves psychoanalysis to be a body of bad psychology it does not follow that it is a bad therapeutic procedure, and vice versa. Similarly, one can even contend that it is neither good psychology nor good therapy, with which I do not agree, and conclude that it is a good method of psychologic investigation. As a fact, Freud himself is of the opinion that the greatest value of psychoanalysis lies in the method. Knowing how frequently patients recover through suggestion and other procedures, it seems that the success or failure of treatment is not proof of the validity of psychoanalytic psychology and that failure does not invalidate the method.

The other point to which I wish to call attention is that practically everything which constitutes psychoanalysis, certainly 95 per cent of it, was born in the mind of Freud. Now, a great many eminent and able men, among whom one may mention Abraham, Ferenczi, Jones, Brill, Jelliffe and Deutsch, not to include dissident analysts, such as Ranke, have practiced and worked and yet contributed little or nothing to the fundamental concepts of psychoanalysis. Any term that may be mentioned—the id, the ego, the superego, repression, regression, transference or the Oedipus complex—all were contributed by Freud alone. The legitimate question therefore presents itself: Why have not others added something to the structure of psychoanalysis? To say that Freud is a genius is true, but geniuses have made contributions to other fields of medicine and were followed by other workers, who continued to make contributions. Psychoanalysis alone has remained what Freud made it. It seems to me that therein lies a fundamental point, namely, that Freud has stated all there is to be said on the subject. He invented or discovered a method, and there is little more to be added. He has given of his great intuitive wisdom and his equally great poetic imagination, for there is no doubt that Freud is a great poet. It was his exuberant imagination combined with his deep intuition and his insight and ability to see beneath the surface which made it possible for him to create. He has given a psychologic

language, which has permeated practically all thought. But the method having been given, all one can do with it now is to apply it. It is, then, in the field of applied psychoanalysis that workers have made contributions.

I have already said that therapy can be divorced from the method. In essence it cannot be divorced because the method itself is therapeutic. If one does not practice psychoanalysis but utilizes the psychoanalylic method he not only will gain an insight into the patient's problem and behavior but, if the latter is at all receptive, will be able to convey his own insight to the patient. It is in this way that the method becomes therapeutic. My opinion is that the value of psychoanalysis lies not so much in its comparatively narrow therapeutic application, not so much in the validity or nonvalidity of the body of psychology but in the superb methodology and the deep insight into the conscious and unconscious working of the human mind which it offers.

As to its dangers, I do not believe that there are grave causes for worry. Psychoanalysis cannot destroy character; it cannot make saints out of reprobates or devils out of saints. The wise and psychiatrically well trained analyst will not continue to analyze a patient with schizophrenia if there is danger that the psychosis will break out into violent dementia praecox. Nor will he analyze depressions and precipitate suicide. As to ruining the characters of children, that danger, too, is not imminent. Actually, psychoanalysis has given more insight into the behavior of children and helped more with child guidance than any other available body of psychology.

DR. A. A. BRILL: I believe that Dr. Hyman's paper has been ably discussed by Dr. Kubie and Dr. Wechsler. I do not think there is anything more to say, except that I think that the conclusions given in this paper are altogether unjustified. The paper does not really tell anything new. I might add that I am sure I never analyzed any of the patients referred for analysis by Dr. Kessel and Dr. Hyman.

Dr. Sachs has always been consistent in his attitude. In his own gentlemanly way, he has always been an opponent of what he calls the "analytic doctrines." Every once in a while, for the last twenty-nine years, Dr. Sachs and I have met on this platform and have expressed our differences regarding Freud's doctrines, but at the last meeting of the New York Neurological Society, when the question came up of electing Professor Freud to honorary membership in the society, Dr. Sachs arose and proposed him for membership. I am glad to say that Professor Freud was unanimously elected. So it will be seen that, in spite of the fact that he is mistaken about a great many freudian theories, Dr. Sachs does recognize Freud's valuable contributions to psychopathology. Dr. Sachs repeated this evening the same arguments which he used with me in 1910, namely, that Freud claims that everything is sexual, a mistaken idea held by many others. Neither Freud nor any of his pupils has ever made such claims. From the present discussion about the unconscious and the other freudian mechanisms mentioned by Dr. Kubie and Dr. Wechsler, it is clear that there is more to the freudian doctrines than sex in the popular sense. If I had the time, I am sure that I could convince this audience, certainly the majority of it, that there is such a thing as the Oedipus complex and that there is nothing mysterious or shocking about the earliest adjustment of the child to the parents, which Dr. Sachs thinks is so terrible.

DR. SACHS: Tell the members what it is.

DR. BRILL: I wish I could, but my time is limited to a few minutes, and I have a great many things to say. Dr. Sachs' objections to the present doctrines of psychoanalysis have been repeatedly answered. If I had the time I should be glad to take up all his arguments and show that he is wrong, but, as we have argued for twenty-nine years, I doubt whether I could convince him. Freud has just celebrated his eightieth birthday, and, as was pointed out by Dr. Kubie, his erstwhile opponents abroad have joined in paying tribute to him. This took place not only in Vienna but in Paris and other places in Europe and Asia. It was a great tribute to his genius that on his very birthday he was elected an

honorary member of the American Psychiatric Association, the greatest body of active psychiatrists in the world, and that they congratulated him by cable. I should like to know whether all these scientists in Europe and in the United States are just babies, who know nothing about mental mechanisms. Incidentally, Dr. Sachs always mixes up psychiatrists and psychoanalysts.

DR. SACHS: Psychoanalysts never make any distinction.

DR. BRILL: They do. I should like to know why all the psychiatrists, all the scientific organizations, which were in the beginning opposed to psychoanalysis and to Freud, are now on his side? To be sure, some still criticize some of Freud's doctrines, but they all admit he has contributed an enormous amount to psychopathology. In fact, he has rewritten the whole subject of psychopathology. Psychiatry was a sterile science and would have remained so if it had not been for Freud's contributions; so what is the use of arguing such minor points as were brought forth this evening? The world has given its opinion. Freud has always stood for his ideas because he believed that they are true. Dr. Wechsler mentioned that other psychoanalysts have not contributed anything new. That is true, and I should explain it by saying that the ideas which Freud gave have opened up so many vital problems that it will take at least twenty-five years more to digest them. We who are really his pupils hardly do more now than learn his principles and apply them to clinical material. Dr. Hyman says that most of the patients with psychoses were not benefited by psychoanalytic treatment. Freud has never advised any one to apply psychoanalytic treatment in the psychoses. He frequently repeated that the psychoses were, for the present, inaccessible to psychoanalytic treatment. But progress is being made in their treatment. Their deeper structures are now known and a prophylaxis is being developed. Dr. Hyman admits, however, that in 1 case homosexuality was cured by psychoanalysis. I could cite half a dozen such cases in which I cured this condition. It is a pleasure to see these normally adjusted persons, who were formerly miserable and were designated as degenerate, now happily married and leading normal and useful lives.

Dr. Sachs is right when he claims that sex is stressed. But Dr. Sachs must not forget that the civilized world was sexually obsessed long before Freud was heard of. How Dr. Sachs can claim that analysis "makes people crazy" I cannot understand. Dr. Sachs' concept of mental disease is singular, to say the least. One may ask why such persons come for analytic treatment. Dr. Sachs need entertain no fear for the future of the children. I am sure that with the sex enlightenment gained from Freud's contributions the next generation will do away with a great deal of sex obscession, from which the world has been suffering since the beginning of civilization.

I may sum up by stating that it is absurd to say that anything done by a psychoanalyst can do harm. There are, of course, charlatans in psychoanalysis, as in every branch of medicine, but any one who masters Freud's principles and applies them expertly can do only good.

DR. ISRAEL STRAUSS: It seems to me that the discussion tonight of the merits of psychoanalysis is much out of place, when the eightieth birthday of Freud is being celebrated. I am convinced that when all have passed into the Great Beyond and have been forgotten, Freud's name and contributions to civilization will live.

The paper which Dr. Hyman read tonight consists of two parts. The part regarding the value of analysis as a therapeutic procedure is favorable to psychoanalysis. I do not know of any psychoanalyst, except Dr. Brill, who will treat a patient with schizophrenia or with manic-depressive insanity. He has done this carefully in the cases he has reported, and his report shows that the patients were benefited. When a person who has schizophrenia stays in the hands of a psychoanalyst for several years there must be a reason. The family must be one that is able to stand the economic strain and is willing to do so, for that family has undoubtedly brought the patient to a psychiatrist who told them of the hopelessness of the condition and they have sought any method which seemed to them

to offer hope, merely because it was an active procedure. I do not blame such a family, nor do I blame the analyst if he is willing to give comfort to the family, when as most practitioners know, the disease may be hopeless.

In judging the effects of psychoanalysis by its therapeutic results, one is in the same position as in other branches of medicine. One is often accused by persons of harming them. I have treated patients and have heard afterward that I hurt them and that some other physician did them "a world of good." I know that what I did, using my best judgment, was harmless. I have even performed a lumbar puncture which was supposed to have started the development of an incurable disease; so the judgment of the patient or of his family as to the therapeutic result is often a dangerous criterion. I think that Dr. Hyman has shown in his cases, other than those of the psychoses, that many of his patients have been benefited, and I know there are patients today that no other form of investigation would help.

As to the economic situation, the physician must manage that. Dr. Kubie has spoken of the difficulty of handling the neuroses among the poor. There are at the Mount Sinai Hospital two clinics, each held three days a week. Each morning there is a clinic, and almost every physician in those clinics is a psychoanalyst. My associates and I cannot use orthodox psychoanalytic methods in the clinic. Naturally, we cannot treat patients in the way they should be treated by that method. But we use the psychoanalytic approach, and this opens up to the analyst data which he can utilize with other methods; the success of that technic is excellent.

As to private patients, I must confess this: I have found among the younger psychoanalysts a number of physicians who have analyzed patients four or five times a week, sometimes even in the evenings in the case of those who are employed during the day, for a fee as low as $60 a month. If that is excessive, I do not know what a moderate charge is. I have had a number of such patients, and I have been able to help these young analysts get on their feet—get their training and their experience. One difficulty, which I state candidly, is in trying to have the men who leave me trained in psychoanalysis. They secure training in neurology and neuropathology. They must have a certain amount of training in psychiatry, and after they leave me they often go to an institution where they learn some psychiatry, particularly the diagnosis of psychiatric conditionss and the treatment especially of the psychoses. I want them trained then in psychoanalysis. I do not want them trained to the extent that they can be stamped on the back, so to speak, so that they can get into a psychoanalytic society, but I wish them to have a working knowledge of psychoanalysis. If they want to go further afterward and become pure, unadulterated analysts, I am willing for them to do so. My difficulty comes in finding teachers in New York who are willing to take them for a moderate fee. I think the New York Psychoanalytic Society must meet that situation. It cannot remain a closed corporation. One forgets, however, that the New York Psychoanalytic Society has been forced a little in the situation, for great pressure has been put on it to train lay analysts. I do not know whether the society has trained any lay analysts.

DR. KUBIE: It was decided not to take them.

DR. STRAUSS: I take my hat off to the society. But it is one problem to which I hope the New York Psychoanalytic Society will attend.

My chief, for whom I have the deepest affection, to whom I owe a great deal and with whom I have worked for years, never agrees with me on this question of psychoanalysis. We are far apart on it. It is known—even psychiatrists who are not psychoanalysts will say—that the formative period in the child, anywhere up to the age of 6 and 7 years, is the danger period. If one is going to prevent the development of a neurosis in the adolescent or in the adult, one must start with the child who shows indications of it.

DR. SACHS: By talking about sex to it.

DR. STRAUSS: One may have to talk about sex in a way, but when one talks about sex with the child, one must bear in mind how much it can understand. One may also have to discuss sex with the parents of the child and make them understand the sex problem as it relates to the child.

DR. H. T. HYMAN: I am a therapeutist, and my approach to this problem was naturally circumscribed by my own limitations. Consequently a great deal of the discussion that followed my paper, so far as I am concerned, is beyond my province to answer at this time; I am tremendously appreciative of the discussion which was aroused. If this paper does nothing else but bring forth frank and honest discussion such as this, it will certainly have justified its purpose.

I am sorry that Dr. Brill thinks that the paper is unjustified. I do not like to engage in badinage at this time, but I shall say this to Dr. Brill: He is a pioneer in freudian therapy in this country, and all owe him a tremendous debt. The contributions of Freud are certainly to be classified among the great contributions of medicine. Dr. Brill has now practiced, I think, for twenty-nine years. In this period a tremendous amount of material must have passed through his hands. I hope he will at some time present his collected material. If he should, a paper such as mine would be unjustified, and it would not be necessary for those who are therapeutists to attempt to get some kind of tangible data on that form of therapy. As to my paper being out of place because it is Freud's eightieth birthday, that needs no comment. No paper is out of place in medicine that brings forth frank and honest discussion. Some of the arguments tonight seem rather ludicrous to me, coming from men who are psychologically trained. The argument that freudianism is worth while because Freud has gained so many honors and so many have praised him is as silly as that Hitler is a great man because nobody else in Germany ever amassed so many votes. That is not the sort of reasoning which would impress practitioners with patients to refer. The physician has an obligation when he refers a patient, which is to see that the patient receives some type of aid. The methodology, the technic, is usually beyond the province of the practitioner. One does have the obligation to send the patient to the specialist who will say what he can or cannot accomplish. I think if one could get definite data from the American Psychoanalytic Society, if a register were formed, similar to the Bone Registry for the Sarcoma Group, and if that register at the end of five or ten years were published, with the results obtained one would have a fair method of guiding one's patients in therapy.

The difference of opinion that appears here is interesting. As a practitioner, I have seen this problem from many points of view. The group of analysts naturally see good results when the patients leave their hands; they rarely see them thereafter. The neurologists see patients who have failed in analysis and have then sought other forms of therapy, just as the analyst must see any number of patients who have failed in the hands of the practitioner and neurologist. Men in institutions say that they never see a good result. The answer is obvious: If the patient had had a good result he would not have gone to the institution. These practitioners must see only bad results, in consequence of which they challenge this method. A forum such as this will bring together diversities of opinion and in that way will prove that papers such as mine are never really unjustified and never out of place.

PSYCHOSIS ASSOCIATED WITH CARDIAC DECOMPENSATION AND THE SYMPTOM OF ANXIETY. DR. JOSEPH WORTIS (by invitation).

In a study of 51 cases of psychosis associated with relatively uncomplicated heart failure, it appeared that a fairly typical syndrome consisting of confusion, anxiety and delusions of persecution occurred. Thus, in an unselected series of 26 patients, 25 were confused, 20 were apprehensive, and 23 had delusions of persecution. The two key symptoms of this type of psychosis were the confusion and the anxiety.

These patients could not make accurate perceptions or integrate them into orderly patterns. They had hallucinations and delusions, especially at night, and

the delusions were usually terrifying. But the most striking and interesting symptom was the anxiety. Not only were the patients in a more or less constant state of fright but their susceptibility to fright was much increased. A patient, for example, developed fear amounting to panic when approached with a syringe for a blood specimen. If the patient were not very confused at the time, he said: "I feel afraid of the needle." If he were confused he might mistake the syringe for a gun and the physician for a soldier; the result was a delusion of persecution. The delusions of persecution in these cases were a joint product of the anxiety and the confusion.

What caused the anxiety? At first thought it would seem that patients were frightened because they knew that they were seriously sick, but most of the patients did not realize that they were sick or even that they were in a hospital. Or it might seem that the patients were frightened by their feeling of helplessness, but one sees so many helpless patients who are not frightened; the explanation is not adequate. Finally, it might seem that the patients were frightened by their own terrifying delusions, but this is only an evasion of the question. Why are the delusions terrifying?

The conclusion seemed unavoidable that the anxiety in these cases was not caused by psychologic factors, that is, by anything outside the organism, but by some disturbance within the organism itself. The anxiety was a body state, without adequate motivation. Unmotivated depression is familiar to most persons, but the existence of unmotivated anxiety is less widely recognized. Except that one is dealing with a different mood, the state of affairs seems to be similar. A depressed patient attempts to justify his depression by finding reasons for it. If he is confused his reasons may be absurd, but he will always feel the need of justifying his mood. A patient in a state of anxiety will attempt to justify his mood in the same way.

Freud, in his classic paper on the anxiety neuroses, written forty years ago, described the anxiety in his cases as a subjective state of physical tension of organic origin. But though it was organic in origin, it nevertheless influenced the psychic life, so that feelings of anxious expectation and hypersensitivity to pain and innumerable fears arose. This explanation may be applied in the cases in my series as well. Since the symptom of anxiety in my patients appeared and disappeared with the signs of congestive failure, the conclusion seems justified that the anxiety was a body state somehow involved in the process of heart failure.

One could venture to say that the patients acquired an increased excitability of the nervous apparatus from anoxemia. But that would be only a supposition. The clinical fact would be that the patients were overacute and overresponsive. Trivial sensations or events took on the proportions of a threat to them: they jumped at the sound of a closing door or started when another patient moved his arm. All their latent or dormant fears were aroused.

Nineteen of the 26 patients could be traced after a period of two years. Of these 16 had died, in most cases during or soon after the period of observation. Two of the remaining 3 were still seriously ill and psychotic, and only 1 was said to be improved.

The high mortality rate in this series indicates that the psychosis is a sign of bad omen. It indicates a failure of the central nervous system, following on and complicating the failure of circulation. The elaborate physiologic mechanism called into play to compensate for the deficiency of circulation has broken down, and the course thereafter is downhill.

One arrives at two main conclusions: (1) Anxiety can be provoked by physical disease, and (2) the combination of confusion and anxiety may induce delusions of persecution. Cardiac psychosis thus calls attention to a fundamental psychologic mechanism and furnishes at the same time a well circumscribed condition in which the physical or physiologic basis of anxiety can be studied.

DISCUSSION

DR. S. BERNARD WORTIS: I want to congratulate Dr. Joseph Wortis on his presentation of interesting material. As I understand his conclusions, he stresses

the fact that cardiac psychosis is uncommon, of grave prognostic omen and characterized by confusion, anxiety and delusions of persecution. One must remember that the cases he has reported were selected from a group of patients with severe cardiac decompensation in psychiatric wards. Wyckoff has shown that in about 8 per cent of cases of cardiac involvement in hospitals there are mental symptoms. Many patients with cardiac trouble associated with mild mental symptoms do not enter a psychiatric hospital.

The prognosis is not always grave in these patients with mental confusion. According to the work of Harrison and Grollman, patients suffering cardiac decompensation with dyspnea and considerable edema usually have a better prognosis than patients who are free from edema. Likewise, in cases in which the dyspnea is equally severe the prognosis is better when hydrothorax or ascites or both are present than when these manifestations are absent.

Delusions of persecution are not peculiar to the cardiac psychosis. They were found by Bowman and Raymond (*Am. J. Psychiat.* **11**:111 [July] 1931) to occur in 56 per cent of cases of schizophrenia and in 20 per cent of cases of manic-depressive psychosis. Furthermore, Wolff and Curran (Nature of Delirium and Allied States: The Dysergastic Reaction, ARCH. NEUROL. & PSYCHIAT. **33**:1175 [June] 1935) found that delusions of persecution and anxiety occur regularly in a great variety of symptomatic psychoses associated with alcoholism, toxic metallic poisonings, infectious diseases and even carbuncle.

The psychic symptoms of mountain sickness may occur in persons with severe anoxemia. Harrison observed and studied the arterial blood of 2 such persons. Both were sleepy, anxious and apathetic. One experienced unconsciousness and loss of sphincter control. The arterial blood showed less than 70 per cent saturation with oxygen in each patient. In each instance increase in the oxygen saturation was associated with prompt improvement in the mental symptoms. Oxygenation of the blood alleviates the mental symptoms of some patients with cardiac psychosis.

Other symptoms of cardiac decompensation, such as unconsciousness, lethargy, perseveration of speech and movement and depression, are seen in these patients. Many factors undoubtedly enter into the causation of the symptomatology, such as biochemical changes in the blood, anoxemia, hydremic states of the body and anemia. Some cardiac psychoses are undoubtedly due to anoxemia (arising from deficient oxygenation either of the blood or of the brain cells). Cardiac decompensation may bring out a latent psychosis.

Anoxemia of the brain may produce confusion and anxiety in some cases of cardiac decompensation. It appears to me that one must consider the anxiety and confusion as liberated psychic patterns. Fears and anxiety feelings are probably ingrained but latent in each person and can be freed by disease or dysfunction of the body or brain. If many kinds of intoxication or infection can produce anxiety and delusions of persecution, this must indicate that experience and fear patterns are written into the brain during life and may be released also in the event of severe cardiac decompensation. Therefore I wish to emphasize that there is probably no one mental syndrome which is exclusively specific for the patient with cardiac decompensation; that is, the psychosis must certainly be largely dependent on each individual patient's psychobiologic endowment. A helpful way to measure the validity and frequent occurrence of the syndrome Dr. Joseph Wortis has alleged as characteristic would be to make a psychiatric study of a control group of patients who had severe cardiac decompensation but were not considered sufficiently ill mentally to be transferred to a psychiatric ward.

DR. KARL M. BOWMAN (by invitation): The discussion of mental symptoms in these cases of cardiac decompensation which Dr. Wortis has described is, I think, an excellent summary of the type of mental disorder which one sees under such conditions, but one of the first points to consider is whether the symptoms are specific for cardiac conditions or whether the symptomatology is merely that of most toxic and infectious types of disorder. In a large number of cases of infectious and toxic conditions of various sorts, particularly those due to alcohol, one will find

that at least two of the symptoms are present, namely, confusion and fear. The cases presented here are highly selected as far as the mental symptoms go, for the patient with cardiac disease in the general hospital who becomes stuporous or has a quiet type of psychosis is not transferred to a psychiatric hospital. The psychiatrist is constantly aware of the fact that many mental patients are treated in general hospitals. The distinction between the psychiatric hospital and the general hospital is not that the psychiatric hospital treats mental diseases and the general hospital does not but that when the mental symptoms of a patient in the general hospital are such that they disturb other patients or make it difficult to care for him he is promptly sent to a psychiatric hospital. Hence, the type of condition in the psychiatric hospital is not a sample of the kind of mental disease which is associated with any particular type of physical disorder. Some patients with cardiac decompensation do not so much show fear as stupor and other definite mental symptoms. However, the type of picture which Dr. Wortis has reported is classic in cases of decompensated heart.

Dr. Wortis considers that the prognosis in these cases is bad, and it is fair to say that whenever a psychosis complicates an organic process the prognosis is worse than it would have been if there had been no psychosis.

In regard to the question of the incidence of mental symptoms in cases of cardiac decompensation, the figures given by various authors do not have much value for the reason that nobody knows what is meant when it is said: "The patient shows mental symptoms." One clinic may have 10 per cent of patients with cardiac disease who show mental symptoms, whereas another clinic may have 50 or 60 per cent.

It has been my experience that in cases of this type morphine has great value. While in general morphine is an undesirable drug for patients who are excited and overactive, the patients with cardiac decompensation represent an exception to the rule. In a number of cases of this sort the use of 0.5 grain (0.324 Gm.) of morphine sulfate intravenously will produce immediate relief. The patient will go to sleep, remain quiet, sometimes for three or four hours, or even longer, and wake up greatly benefited. Sometimes the acute symptoms of the psychosis will have disappeared.

DR. JOSEPH WORTIS: Dr. S. Bernard Wortis has suggested that the psychosis may be attributed to anoxemia—that anoxemia is the cause of the mental changes. Actually, however, anoxemia is almost never uncomplicated. With anoxemia, especially when associated with heart failure, one often finds, for example, an increase in the lactic acid content of the blood and resulting acidosis. The anoxemia itself may be compensated for by an increase in the hemoglobin and in the respiratory rate, so that failure of the respiratory center or an inadequate erythrocyte response may be responsible for the anoxemia, or some vascular deficiency may be the final factor which makes the difference between an effective and an ineffective blood supply. I should hesitate to attribute the psychosis at the present stage of knowledge to any single factor. It is interesting to note the result of oxygen deprivation on normal subjects. This has been studied at Columbia University. The usual response to oxygen deprivation is apparently not anxiety but euphoria resembling a state of drunkenness (McFarland, Ross A.: The Psychological Effects of Oxygen Deprivation [Anoxemia] on Human Behavior, ARCH. PSYCHOL., no. 145, 1932). It is questionable how far one can blame oxygen deprivation for the picture. Even if it is assumed that anoxemia is the basic cause, it is probable that a constellation of other factors is involved at the same time.

Regarding the specificity of the picture, I should not like to make any strong claim that the picture is specific for the mental changes in cases of heart failure. It is easy to find similar mental changes associated with other internal diseases. However, I think that the picture described is fairly typical for cardiac psychosis and that the intensity and frequency of the state of anxiety are striking, as compared with the pictures associated with other internal diseases. But even if the picture is not specific, I think that cardiac psychosis has a special significance; for in these cases a psychosis is shown which is due not to any external influence, not to a toxin or to alcohol but to a purely internal derangement of function.

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

Regular Meeting, May 21, 1936

STANLEY COBB, M.D., *President, in the Chair*

PSYCHONEUROTIC ASPECTS OF OBSESSIONAL NEUROSIS. DR. HANNS SACHS.

This article will be published later.

BRILLIANT VITAL RED AS AN ANTICONVULSANT. DR. STANLEY COBB, DR. MANDEL E. COHEN and DR. JOSEPH NEY, Chicago.

At different times during the past ten years the problem of cerebral anoxemia and its relation to certain convulsive phenomena has been studied in the laboratories of the department of neuropathology of the Harvard University Medical School. (Gildea, E. F., and Cobb, Stanley: The Effects of Anemia on the Cerebral Cortex of Cats, ARCH. NEUROL. & PSYCHIAT. **23**:876 [May] 1930; Lennox, W. G., and Cobb, Stanley: *Medicine* **7**:229, 1928). A search was begun in 1935 for a stain which might act as an indicator of slight and early asphyxial changes in the nerve cells of the brain and spinal cord. It was observed that neutral red injected intraperitoneally in mice could be observed in the large ventral horn cells of the spinal cord. This observation was definite, though rare. Asphyxia of the mice with nitrogen caused no increase in the amount of the dye taken up by the ventral horn cells; so we decided to see what great motor activity would do. Accordingly, one of us (J. N.) performed a series of experiments in which convulsions were induced in the mice after the intraperitoneal injection of neutral red. It was noticed that the action of the convulsant was more or less inhibited by the dye. Three convulsants were used. Triphenylphosphite gave all the animals convulsions, whether or not they had the previous injection of neutral red, but the animals which had such injections showed a marked delay in the time of onset of the convulsions: all of them lived longer. Camphor liniment was given to 20 mice, of which 10 received a previous injection of neutral red and 10 did not. Both groups of animals had many convulsions, but in those protected with the dye the convulsions were conspicuously delayed. Picrotoxin, on the other hand, caused immediate convulsions, whether or not the dye had been previously given. In fact, the mice that had received injections of neutral red seemed to fare worse in the long run than those that had not.

A series of experiments was then carried out on rabbits. In each animal the threshold convulsive dose of camphor liniment was determined by injections repeated at intervals of two or three days. Each animal was then given two or three intravenous injections of brilliant vital red (disodium disulfonaphtholazotetramethyltriphenylmethane) until the sclera, skin and mucosa became conspicuously red. The convulsant dose of camphor was then given and the result noted. Rabbit 6 had no convulsions after the first three injections of vital red. Rabbit 9 showed a decrease in the severity of the convulsions after small doses but did not cease having convulsions until a massive dose of 30 cc. of the dye was injected. Rabbits 10 and 11 experienced no inhibiting effect from the preliminary injection of the dye but stopped reacting to the convulsant after large doses (30 and 29 cc., respectively, of a 1 per cent solution). Rabbit 12 showed less convulsive reaction after two small doses of dye. Rabbit 13 reacted much like rabbit 9. In summary, all 7 rabbits, after being thoroughly stained with the brilliant vital red had a decided resistance to the convulsive action of camphor.

Experiments with strychnine were undertaken by Dr. A. E. Rauh. He gave to 12 white rats doses of strychnine sulfate sufficient to produce spontaneous convulsions. All the animals died. Equivalent doses of strychnine were given to 13 rats after one intravenous injection of brilliant vital red. Of the 13 rats only 3 showed spontaneous convulsions. Seven of the remaining 10 rats showed convulsions when disturbed by such stimulation as pinching the tail; 4 of the 10

died, and 6 survived. It appears, then, that the convulsive action of strychnine is also somewhat inhibited by the intravenous administration of brilliant vital red.

In the light of these experiments it seemed justifiable to try the dye on patients with epilepsy.

CASE 1.—A boy aged 14 years, who was microcephalic and feebleminded, had had from 10 to 40 seizures a day for two years, and in the hospital the number of seizures averaged 20 in eight hours. Four daily intravenous injections of a 1 per cent solution of brilliant vital red caused a sharp drop in the number of seizures. During the next ten days he received injections of physiologic solution of sodium chloride as a control. The seizures again increased in number. Then for eight days he was given daily injections of the dye. He became conspicuously red, and the number of seizures declined. At home this improvement held for three weeks, the seizures being fewer and milder. They then gradually returned. At the end of two months the red tint of the skin is only just discernible.

CASE 2.—A boy aged 7 years, with cerebral atrophy, feeblemindedness and epilepsy, had from 12 to 20 seizures daily, despite medication with phenolbarbital. Administration of brilliant vital red was begun on the ninth day of observation and was continued until he was the color of "alizarin pink" (Ridgway, Robert: Color Standards and Color Nomenclature, Washington, D. C., published by the author, 1913). At this time the fits began to decrease in number. On the twenty-eighth day of the study albumin and dye appeared in the urine. On the forty-third day the patient had his last convulsion; he had had no more up to the three hundred and thirty-first day.

CASE 3.—A white girl aged 10 years, with epilepsy of the pyknoleptic type, no neurologic signs and a mental level within normal limits, had had frequent convulsions for five years. For two months before her admission to the hospital the number of convulsions was increasing in spite of the use of phenolbarbital, 2¼ grains (0.146 Gm.) daily, and the attacks were becoming more severe. Phenobarbital was discontinued, and brilliant vital red was administered. In spite of repeated large doses of the dye, there was no evidence of renal irritation, and no dye appeared in the urine. The skin, however, became extremely red, the color of "shrimp pink to geranium pink" in Ridgway's standard of colors. The number of convulsions did not decrease, but when administration of phenobarbital was added the seizures became fewer and milder. The patient has not fallen in an attack since she left the hospital. Improvement held for two months, at the end of which all but a trace of the red pigment in the skin had been lost.

CASE 4.—A boy aged 16 years, with mental confusion and frequent attacks of grand mal of unknown etiology, had had seizures for ten years. Drugs, dehydration and induction of acidosis had all been tried, without avail. After a period of two weeks as a control, during which there were 6 convulsions in each week, 195 cc. of a 1 per cent solution of brilliant vital red was administered by Dr. W. G. Lennox. In that week there were 14 seizures. In the fourth week 120 cc. was given, and there were 5 seizures. The patient continued to become redder. In the fifth week the patient was given 40 cc.; he was still redder and had no convulsions. In the next week the patient had 3 convulsions, which, according to the father, were mild and were followed by only a short period of confusion. The father noted, however, definite increase of nervousness in the boy.

CASE 5.—A girl aged 2½ years, with status epilepticus associated with diffuse cerebral sclerosis (Schilder's disease?), had had convulsions for fifteen months. There had been about 20 convulsions during the first year of illness. In February 1936 she began to have daily generalized convulsions. Induction of ketosis and sedatives were used in therapy, and there was brief improvement. Encephalograms showed marked cortical atrophy of the frontal lobes. The patient was transferred to the Children's Hospital, where the convulsions were recorded. The number averaged from 10 to 15 a day. Administration of brilliant vital red was begun and continued until the child was "geranium pink" (Ridgway). There then occurred a decrease in the number of spells, until five consecutive days passed in which none occurred. She returned home, and at the last report only 3 slight seizures had occurred in ten days.

CASE 6.—A boy aged 8 years was seen at the Children's Hospital; he had had convulsions on the right side since the age of 2½ years. Birth was with instruments and was difficult. In 1931, when he was first seen at the Children's Hospital, it was noted that the convulsions were always on the right side. An encephalogram showed slight enlargement of the ventricles and subarachnoid space. He was feebleminded, left handed and right eyed. Convulsions were unilateral and were more frequent and more severe at the time of the second admission. Brilliant vital red was administered, and there was an increase in the number of convulsions. The use of the dye was discontinued because it was thought that the boy should have surgical treatment and because he feared the intravenous injections and "put on a show" to avoid them. Operation showed a small area of atrophy in the left frontal lobe bordering on the motor area.

DISCUSSION

DR. TRACY J. PUTNAM: This drug promises to be a valuable addition to the chemical armamentarium against epilepsy. It is rather amazing, considering that epilepsy has been recognized since the beginning of medical history, that there are so few drugs effective against it and that all of them have been stumbled on by chance. An enormous amount of effort has been expended in devising better hypnotics but little in comparing the value of anticonvulsants. The requirements are of course, entirely different.

This is a problem in which Dr. Merritt and I have been interested for many months; it seemed to us that if we were to make a systematic survey of drugs having a greater effect on irritability and motor phenomena and less hypnotic effect than those at present available we might well begin with some of the less toxic phenol compounds. This is suggested not only by the fact that phenobarbital is the most effective of the barbiturates but by work that Dr. Tinsley Harrison has done on the mechanism of uremia which makes it evident that phenol compounds in general have exactly the sort of motor depressant effect that we should like. The only difficulty is that they are injurious to the kidneys. I am particularly interested to observe that the compound described tonight consists of a string of benzol rings and possibly is comparable to some of the endogenous conjugated phenols. I wish to ask if there has been any evidence of renal irritation or decrease in renal function and also in what form the substance is excreted.

DR. BRONSON CROTHERS: As many of these children are so young, should they not be given rigid psychologic tests at intervals? Both patients I have studied seemed more alert after the drug had taken effect. For a patient whom my colleagues and I observed, who came from New Haven, Conn., and was studied by Dr. Resell's group before he came to us, and also for other patients, we have accurate records.

DR. J. B. AYER: I can testify as an onlooker in 2 of these cases. The changes in character were observed in the ward. Bad manners and the character changed markedly. I wish Dr. Cobb would tell more about the histologic changes. Has the dye a selective affinity for motor cells? This is a rather extraordinary experiment, a clever application of observed fact, and Dr. Cobb deserves great credit for the correlation of fact and theory.

DR. STANLEY COBB: As to the substance having any hypnotic effect, that has been already answered. The patients become more active; all seemed rather more alert. Perhaps that is one effect of the vital red. It is excreted largely in the feces and in the wax of sebaceous glands around the edges of the eyelids and in the hair. It is a mild irritant. It appears in the urine only after injection of large amounts. A little albumin and a few red cells and casts are present in the urine. The histologic work is preliminary and needs much more study. If the specimens are hardened in formaldehyde or alcohol, one washes out the dye. One must use fresh tissue and examine it on a warm stage. In this way I have often seen the dye in the spinal anterior horn cells and once in the large motor nerve cells of the motor area of the hemisphere. Perhaps one can work out a new method of hardening with liquid air.

PHILADELPHIA NEUROLOGICAL SOCIETY

Regular Meeting, May 22, 1936

FREDERIC H. LEAVITT, M.D., *President, in the Chair*

HYPERTROPHIC INTERSTITIAL NEURITIS OF DÉJERINE AND SOTTAS. DR. A. M. ORNSTEEN and DR. PAUL SLOANE.

L. H., a Negress aged 53, married, was admitted to the medical service of the Philadelphia General Hospital on Oct. 8, 1935, with the complaint of epigastric pain that had been present since 1931. The pain was occasionally, but not always, related to the intake of food, did not radiate and was associated with vomiting of mucus stained with bright blood. A diagnosis of chronic cholecystitis was made and confirmed at operation. Shortly after the cholecystectomy, however, the pain returned in all its original severity.

A neurologist was then called in consultation because it was observed that the patient had bilateral foot drop and absence of knee jerks. A review of the history showed that for a number of years the patient had complained that her feet turned in while walking. One year ago she suddenly began to complain of sharp pain in the right instep, followed by numbness and weakness of the right leg, so that she was unable to support herself on it. The leg was treated with rest and massage and showed temporary improvement in power. The weakness and numbness then spread to the left leg, and the patient became entirely chair-ridden. She then began to complain of numbness, weakness and cramplike pains in both hands. This condition had continued to the time of examination.

Of interest in the past history was the occurrence of typhoid at the age of 10 years, pneumonia at 38 and mumps at 40. Cesarean section was performed at the age of 26, after which the patient ceased to menstruate. There was no familial history of nervous or paralytic disorder. The patient had been married thirty-four years and had 3 children. There had been no miscarriages.

Neurologic examination revealed the following signs: The pupils were equal and regular; they were fixed to light but reacted promptly in accomodation. The deep reflexes in the upper limbs were active and equal on the two sides. The knee and ankle jerks were absent bilaterally, even on reenforcement. No response of the big toe was obtained on plantar stimulation on either side. The right hand grasp was weak as compared with the left. All movements of the wrists were weak, particularly on the right side. Power in the proximal portions of the upper limbs was intact. There was likewise no weakness in movements of the hips but some impairment in the flexor muscles of the knees and more in the extensor muscles. There was bilateral talipes equinovarus. The patient was able to extend the ankles partially. The toes of the left foot could be partially extended, but not those on the right. There was also weakness in the plantar flexor muscles and the invertor and evertor muscles of the feet bilaterally, but more on the right. Atrophy of the intrinsic muscles of the hands was present, as well as symmetrical atrophy of the legs below the knees. There was a glove and stocking type of hypesthesia in all modalities below the wrists and knees, the right side being again more affected than the left. The ulnar and external popliteal nerves on both sides were thickened and palpable but not tender. There was marked ataxia on both sides in the finger to nose test with the eyes closed. No scoliosis was present. Electrical reactions were not obtained from the muscles or nerves of either leg. Sections of the right external popliteal nerve taken for biopsy were studied by Dr. Helena Riggs. They showed a picture typical of hypertrophic interstitial neuritis.

Laboratory tests gave essentially normal results, except for moderate secondary anemia. Serologic tests of the blood and spinal fluid gave negative reactions. Examination of the spinal fluid revealed 3 cells per cubic millimeter and no increase of globulin; the colloidal gold curve was 1123210000.

The condition in this case resembles that in Charcot-Marie-Tooth type of progressive muscular atrophy. The noteworthy features in the case are the onset at such a late age, the absence of familial history and the comparatively rapid course. It is well known, however, that the clinical picture varies within wide limits, although in the original cases reported by Déjerine and Sottas the condition arose early in life and was characterized by familial occurrence. Argyll Robertson pupils and lightning pains may be present or absent. It is questionable whether the abdominal pains for which the patient was originally admitted could have been due to involvement of the posterior roots. The pain, however, was not typical, and the further course indicates that it may have been largely psychogenic. It has not been present for several months.

DISCUSSION

DR. HELENA RIGGS: I shall show slides of the muscle and the nerve trunks in the case described by Dr. Ornsteen and Dr. Sloane and report the autopsy observations in another case from the Philadelphia General Hospital.

The patient I observed was 63 years of age at the time of onset; the condition started with weakness of the arms, drooping of the head and dyspnea. In twelve months weakness of the upper extremities was so severe that the patient had to be fed. At this time the patient was thought to have pernicious anemia, and with liver feeding she felt better. Physical examination a year before her death showed slight exophthalmos and wasting and fibrillary tremors of the muscles of the neck and shoulder girdle. There was paralysis of the pectoral groups and of the shoulder muscles. The lower extremities were relatively normal. Marked vasomotor disturbance was manifested by excessive sweating. At this time the red cell count was normal. The patient died suddenly in vasomotor collapse. Autopsy revealed that the heart, liver, pancreas and stomach were small. The pituitary fossa was normal in size, but the pituitary gland was very small. The bone marrow showed no evidence of changes characteristic of primary anemia. Microscopic study of the voluntary muscles showed extreme atrophy, which had been progressive. The nerve trunks were not markedly enlarged but showed the typical "onion bulb" changes in the nerve fibers. Differential staining showed that this was not due to proliferation of connective tissue. The material resembled rather colloid or mucin. The changes in the nerve trunks were observed also in the third, eighth, tenth and twelfth cranial nerves. The same change was noted in the intramedullary fibers of the third and tenth nerves. In the spinal cord there were almost complete absence of anterior horn cells in the upper thoracic region and axonal chromatolysis in the lumbar region. These changes were present in the cells of Clarke's column throughout. In the nucleus of the anterior colliculus there was severe degeneration of the ganglion cells with gliosis; this may account for the Argyll Robertson pupil reported in many cases.

In this case it is interesting to note that there were numerous embryonic defects. The spinal cord showed a patent central canal, with central gliosis. There were areas of focal absence of the medial coat with formation of miliary aneurysms throughout the arteries of the brain and cord. At one level in the spinal cord there was a small venous angioma in the subarachnoid space, and another occurred in the choroid plexus of the fourth ventricle. These abnormalities, which were congenital, suggest a possible congenital basis for the hypertrophic neuritis.

DR. ALFRED GORDON: Does Dr. Sloane know of any etiologic factor in this case? Several years ago I saw a case in which there was prolonged exposure to cold. How many years after the mumps, typhoid and pneumonia did the trouble commence? Déjerine and Sottas reported cases in which ataxia developed in addition to other symptoms, and at autopsy lesions of the posterior portion of the cord were present. A marked hereditary element seems to prevail in these cases.

DR. PAUL SLOANE: We did not find a definite etiologic factor. There was no history of syphilis, lead or alcohol. The various diseases enumerated in the

patient's history occurred many years before the onset of the trouble. The last disease was mumps, at the age of 40, while the present condition began at the age of 48. The interesting features are the late onset and the rapid progression. In the case reported by LeBruyn and Stern the condition began at the age of 50, the patient dying three years later. In most of the cases reported involvement of the posterior columns was shown. The case of LeBruyn and Stern was an exception in this respect.

LEAD ENCEPHALOPATHY WITH CONVULSIONS. DR. BALDWIN L. KEYES and DR. J. GEORGE MAHARG (by invitation).

It is unusual for a man nearing the age of 60 to recover from lead encephalopathy of sufficient severity to produce severe convulsions, acute psychosis and glomerulonephritis. The question of diagnosis is always difficult unless lead is thought of and searched for, recovery depends on the prompt elimination of available lead and the fixation in the form of insoluble salts of the remaining quantities in the tissues.

A Negro apparently aged about 65 was admitted to the psychopathic ward of the Philadelphia General Hospital without a history on Jan. 30, 1936, manifesting confusion, disorientation, delirium and extreme agitation, with noisiness and thick, slurring speech. Two convulsive seizures occurred soon after, starting in the left arm and quickly becoming generalized; the eyeballs deviated downward and to the right.

Physically the patient was well developed; the eyes and sclera were muddy; there was slight nuchal rigidity; the heart and lungs were normal; the blood pressure was 160 systolic and 90 diastolic, and the blood vessels were sclerotic.

Neurologic examination revealed that the pupils were unequal and irregular, the left being larger than the right. They reacted sluggishly to light. There was a coarse tremor of the tongue, with protrusion in the midline; speech was thick and slurring. The left arm was weak. Sensation could not be accurately tested. The deep reflexes were unequal on the two sides, being more active on the left. No pathologic reflexes were noted. There was incontinence of the feces and urine. Examination of the eyegrounds revealed angiosclerosis and retinal hemorrhages but no papilledema. A roentgenogram of the skull showed normal structure, without signs of pressure or of shift of the pineal body. The spinal fluid pressure was 45 mm. of mercury with the patient in the sitting position.

The Queckenstedt test gave a normal response. Examination of the spinal fluid showed: Wassermann reaction negative, colloidal gold curve 1112221000, sugar 87 mg. per hundred cubic centimeters, chlorides 830 mg., total protein 150 mg., globulin a heavy trace and cells 2 per cubic millimeter. Early studies of the blood showed: hemoglobin content 7.5 Gm. per hundred cubic centimeters, red cells 3,370,000, white cells 19,100, polymorphonuclears 69, eosinophils 6, a shift to the right with the Schilling test, sugar 112 mg. per hundred cubic centimeters, urea 80 mg., carbon dioxide content 43 cc., volume index 0.81, total calcium 11.1 mg. and serum chloride 615 mg. The Kahn reaction was negative. Urinalysis revealed: acid reaction; specific gravity from 1.012 to 1.019; no albumin, sugar or sediment; total proteins 8 mg. per hundred cubic centimeters, and urea clearance 26 per cent in the first hour and 34 per cent in the second. The Mosenthal test gave fair results.

A number of preliminary diagnoses were considered, including tumor of the brain, syphilis of the central nervous system, diffuse toxic encephalitis and glomerulonephritis with uremia.

A history obtained later was helpful. The patient, whose age was given as 59, had for two years complained of weakness, headache and abdominal discomfort. During the five months preceding his admission the symptoms became gradually more severe, with insomnia and abdominal pain.

For three weeks prior to his admission he was confined to bed because of persistent headache and vomiting. One week before his admission he had a generalized convulsive seizure, associated with incontinence of urine and followed

by stupor and confusion. For three days he had pain in the chest, without cough or hemoptysis. There was nocturia but no hematuria. On the day of admission to the hospital two severe generalized convulsive seizures occurred and were followed by stupor and delusions. He had had typhoid in early youth; he had otherwise always been healthy and did not take alcohol. He had been employed as a stationary fireman until four years before. Since, he had been a junk collector. The latter occupation suggested lead as an etiologic factor, and it was learned that during the past four winters he had burned discarded storage battery cases for fuel in a dilapidated open heater in his living room.

Following this suggestion, further studies were instituted. A twenty-four hour specimen of urine contained 0.45 mg. of lead per hundred cubic centimeters. The blood showed rapidly increasing anemia, with anisocytosis, poikilocytosis, achromia and pronounced stippling. A lead line on the gums was barely perceptible. The spinal fluid was not tested for lead.

Therapy with a diet high in calcium and administration of calcium lactate and cod liver oil by mouth was instituted. Before the lead fixation therapy was begun the patient was almost comatose; he had to be fed with a tube and was practically moribund. Within twelve days after therapy was instituted the patient was clear mentally and was gaining in weight and strength. He was discharged as recovered on April 16, 1936, and reported to the medical clinic. There were sequelae consisting of weakness of the extensor muscles of the wrists, worse on the left, weakness of the left biceps muscle, atrophy of the small muscles of the hands, worse on the left, masklike facies, lateral nystagmus to the left and slight impairment of hearing.

A further investigation revealed that all members of the patient's family had recently suffered from constipation, abdominal cramps and headache. All had had unpleasant saliva and almost black nasal discharge. One child had a lead line on the gums.

COMMENT.—In all cases of toxic encephalitis of unknown origin, metallic poisoning, particularly that due to lead, must be considered. The importance of the history in diagnosis cannot be overstressed. Prompt calcium therapy is vital. A check on collateral contacts to determine the source of poisoning is important. Dissemination of knowledge concerning risks from this source should be a public health requirement.

DISCUSSION

DR. ROSS THOMPSON: What does Dr. Keyes think is the normal amount of lead in the cerebrospinal fluid? Was the patient's urine collected in a glass vessel?

DR. B. L. KEYES: I do not believe that lead is found normally in the spinal fluid. I assume that the urine was collected in glass vessels, as usual. The urine contained lead. A third blood count showed stippling and poikilocytes. There was a thin lead line on the gums, so faint that it was not at first detected.

DR. F. H. LEAVITT: Apparently, one of the most frequent causes of lead poisoning is the burning of battery boxes. It seems to be a prevalent custom.

HEMIPLEGIA ASSOCIATED WITH PRESENCE OF ABDOMINAL REFLEXES. DR. DAVID NATHAN.

Cases of hemiplegia associated with active abdominal reflexes are sufficiently uncommon to warrant the report of this case. It is true that one finds active abdominal reflexes in cases of infantile hemiplegia relatively more frequently.

All movements of the abdominal muscles in response to stimuli are not identical with normal reflex response, in which the rectus, oblique and transversalis muscles take part in the healthy person. There are cases of inversion in which the opposite side of the abdominal wall responds and others in which the whole side of the abdomen acts *en masse*. Monrad-Krohn (Monrad-Krohn, G. H.: Reflexes of Different Order Elicitable from the Abdominal Region, ARCH. NEUROL. & PSYCHIAT. **13**:750 [June] 1925) stated that deep stimulation may produce reflexes

of the abdominal musculature that are increased after injury of the pyramidal pathway; they are analogous to tendon reflexes and are true stretch reflexes. These reflexes differ from the normal in the following points: (1) There is a long latent period following stimulation; (2) contraction is markedly bilateral, the contraction on the contralateral side being sometimes greater; (3) there may be an accompanying slight flexion of the hip and knee joint; (4) greater stimulation is required to produce response, and (5) tickling sensation, which normally accompanies the abdominal reflex, is absent. Abdominal reflexes are present in normal persons, probably in 100 per cent of cases; when they are not obtained the subjects have flabby or obese abdominal walls or ill developed musculature or are atonic or asthenic. Astwazaturow (Astwazaturow, M.: On the Nature of Abdominal Reflexes, *J. Nerv. & Ment. Dis.* **61**:587, 1925) asserted that the abdominal reflexes depend on a cerebral reflex arc, that they are phylogenetically new acquisitions, that they cannot be obtained in domestic animals and that they are absent in infants and become permanent at the eighth month of life. That is the age when the child learns to assume the erect posture.

Langworthy (Langworthy, O. R.: Mechanism of Abdominal and Cremasteric Reflexes: Collective Review, ARCH. NEUROL. & PSYCHIAT. **24**:1023 [NOV.] 1930), who covered the subject of the abdominal reflex exhaustively, said that the abdominal reflex is primarily initiated by a reflex arc through the spinal segments. After all cerebral control is removed, the abdominal reflexes become active and tend to be bilateral and associated with flexor movements of the legs. The abdominal reflex is part of a widespread defense reflex that protects the vulnerable abdominal wall from injury. The spinal reflex arcs are normally under the control of pathways from the brain; the result of this control is either augmentation or inhibition of the spinal reflex. After injury of the corticospinal fibers, the abdominal reflexes are decreased or abolished. Influences from the motor cerebral cortex normally augment the abdominal reflexes. The motor cerebral cortex normally inhibits the tendon reflexes.

The muscles from which tendon reflexes are obtained are those of the extremities normally exhibiting postural tone. In order that the normal phasic movements initiated in the motor cortex may be carried out, the postural tone of the antagonistic muscles must be inhibited. Therefore a mechanism for this inhibition has been developed in the cerebral cortex. The abdominal muscles, on the other hand, are flexor phasic muscles, which do not exhibit the tonus of the antigravity musculature; moreover, they have no antagonistic muscle groups. The existence of the normal abdominal reflex is dependent on the integrity of the corresponding pyramidal fibers; the abnormal abdominal reflex is one of spinal automatism. The abdominal reflex is strongly developed in forms that have assumed the erect posture.

REPORT OF A CASE

T. Q., a truck driver, aged 35, married, complained of paralysis of the left side and nervousness. Both his parents and 3 siblings were living and well. The family history was otherwise of no significance. The patient had had measles in childhood and pleurisy and pneumonia in 1921. He denied infection with venereal disease or acute rheumatism. He had 4 children who were living and well; the wife had had no miscarriages.

The present illness began on July 20, 1930, when a hemiplegia developed on the left side while he was reading in bed. There was no loss of consciousness; he had not been sick before, and there was no headache at any time. The paralysis has remained unchanged to the present. Now, he is fidgety and nervous, irritable and easily aroused to anger; chilly sensations run up the back, and occasionally there is a feeling of local twitchings (not visible) here and there on both sides.

Examination revealed a thin, wiry, only fairly nourished man, whose station was good and whose gait and attitude were those of left spastic hemiplegia. The pupils were moderately large, equal and regular and were active both to light and in accommodation; all external ocular movements were wide in range; the fundi were normal. There was weakness of the lower left side of the face; the tongue was protruded slightly to the left and was tremulous. There were no

other cranial nerve palsies. The deep reflexes on the left were all present and exaggerated; the abdominal reflexes were brisk on both sides; there were Trömner and Babinski signs on the left. The left arm and leg were spastic; ankle clonus was present. There was general wasting of the left side, with some trophic phenomena. No objective sensory disturbances were noted. No sign of cerebellar dysfunction was noted. The patient was correctly oriented and emotionally labile; there were psychoneurotic symptoms. The Wassermann reaction of the blood was negative. Mitral insufficiency and stenosis were present. The blood pressure was 134 systolic and 80 diastolic. The condition was probably of embolic origin.

DISCUSSION

DR. R. THOMPSON: I was once asked by a medical student how to distinguish between a psychic or defense abdominal reflex and the phenomenon which results from stroking the skin of the abdomen with light touch. It was his thought that the knowledge of an external object coming in contact with the abdominal wall would result in a contraction of the muscles similar to that produced reflexly by light touch. The patient in the present case seems to anticipate each stroke of the object, and possibly some of the response may be due to an instinctive defensive mechanism.

DR. D. NATHAN: This reflex was poorly shown in this case. The abdominal reflex is one that cannot be controlled by reenforcement. When one reeinforces, the abdomen becomes contracted. The umbilicus was pulled to one side. In this case the abdomen was contracted, and the patient, retracted the abdomen in defense. A certain amount of defense reflex was shown here, but there was also reflex movement, which is a true cutaneous reflex. I am certain that the abdominal reflexes are present and equal on the two sides.

MECHANISM OF HEADACHE. DR. TEMPLE FAY.

Scope of Observations.—Direct observations on the exposed human brain, as well as roentgen studies of mercurial injections in the arteries, have indicated a wide latitude of vascular changes in volume and pattern. The correlation of studies on intracranial volume in the light of the Monro-Kellie doctrine and the evidence, obtained from fifteen years of study of the relationships of intracranial volume and pressure, as encountered in states of hydration and dehydration under various pathologic conditions of the brain, have served to establish the fundamental physical properties and changes related to such a mechanism.

With the establishment of a vascular mechanism for pain on the arteries and veins supplying the head, neck and face, a series of studies regarding the preservation of pressure-pain sensibility in areas of anesthesia produced by section of the cranial sensory nerves and upper cervical nerves established that, underlying the peripheral pain pattern carried by the cranial and spinal nerves to the head and face, there is a distinct vascular pattern following the large arteries and veins.

These studies on the sensory nerves were presented by Spiller and me before the American Neurological Association at its annual meeting at Atlantic City, N. J., in June 1926. Attempts to interrupt surgically the vascular pain fibers at various points within the cranial cavity, neck and spinal cord have covered a period of seven years, and the results obtained in the problem of so-called "atypical neuralgia," or Sluder's syndrome, have been presented and published at various times during this period.

Responses to Stimulation.—I have applied faradic stimulation, traction, irritation and heat to the structures within the cranial cavity (with the patient under light anesthesia with tribromethanol in amylene hydrate or local anesthesia(and observed that a sensation of pain similar to localized headache can be produced only when the branches of the meningeal artery are directly involved; the internal carotid arteries, the circle of Willis, the anterior middle and posterior cerebral arteries from the circle of Willis at the base to a point approximately at the level of the sylvian fissure, when the basilar and vertebral arteries have been appropriately stimulated.

Referred pain similar to headache can be elicited by stimulation of the superior sinus from a point approximately underlying the hair line of the forehead to the torcular Herophili, the two lateral and the two sigmoid sinuses.

Great pain is experienced from traction or stimulation of the branches of the venous supply, the tentorium, the inferior straight sinuses and the cavernous sinus, and on one occasion pain was produced by stimulation of the right choroid plexus.

Reference of Pain and Headache.—Stimulation of the arterial tree near the branches of the circle of Willis produced pain referred deep into the eyes and forehead. Stimulation of the middle cerebral artery in the transverse fissure and insular area produced pain which was lateralized to the temporoparietal region; stimulation of the superior sinus produced diffuse pain, regional in character, referred to a point deep in the eyes, especially as the point of stimulation approached the torcular Herophili; stimulation of the tentorial veins and lateral sinuses produced pain referred to the occipital area and deep behind the eyes. Stimulation of the cavernous sinus produced pain referred directly behind the eyes and in some instances toward the jaw.

Stimulation of the common carotid artery at the bifurcation projected pain into the teeth, gums and lips, which was occasionally lateralized to the temporoparietal area.

Stimulation of the jugular vein produced pain in the tongue, gums, teeth, face and occipital area, lateralized to the side of stimulation.

Compression of the jugular vein of the neck, with the lateral sinus and posterior portion of the superior sinus produced occipital headache referred deep in the eyes, when the vascular engorgement reached a point of actual gross tumescence of the dural sinuses.

Generalized headache was produced by increasing the intracranial pressure by means of a buret connected with a spinal needle, allowing distention of the ventricular arachnoid fluid spaces and "stretch" of the arterial vascular tree, the pain produced being relieved by release of the hydraulic distention.

Hyperemia induced in the intracranial cavity by subtraction of spinal fluid below the normal component, such as is obtained by lowering the buret attached to the spinal fluid system and permitting an excess of spinal fluid to be withdrawn, coincident with compression of the jugular veins and the act of coughing or straining, produced intense headache, which may persist after jugular pressure has ceased but is promptly relieved by elevation of the buret and introduction of fluid into the spinal canal, expressing the blood which temporarily has been allowed to distend the intracranial arterial structures.

The pain of so-called "atypical neuralgia" ("lower half headache") and unilateral headache persists after section of all sensory cranial nerves (trigeminal, glossopharyngeal, vagus and intracranial roots), including the upper four cervical posterior roots.

In spite of the total objective anesthesia produced by section of the cranial nerves devoted to common sensation and of the upper cervical posterior roots, a dull throbbing, boring pain may persist, but this is relieved when the patient is subjected to the method of ascending spinal anesthesia (which I presented before the American Neurological Association in 1933), provided that the level of anesthesia is allowed to reach the fifth cervical segment of the spinal cord. This type of pain becomes modified when the anesthesia reaches the third thoracic dermatomere and has practically been obliterated by the time the anesthesia involves the eighth cervical dermatomere, i. e., anesthesia of the ulnar aspects of the hand.

This type of pain, which persists after section of the sensory and cranial root components, disappears after anterolateral chordotomy at the level of the fifth cervical segment of the opposite side. Vascular pain, referred unilaterally to the cranial cavity or deep structures of the face, may be partially, but not wholly, eliminated with proper interruption of the fibers contained within the

vagus sheath, the outer coat of the internal and external carotid arteries and the sheath of the jugular vein; other fibers, however, descend with the vertebral arteries and are inaccessible.

My observations indicate that these fibers may traverse well known pathways of the sympathetic system but do so only to reach their vascular components. Destruction of the sympathetic chain and ganglia and roots in the upper thoracic and lower cervical region may or may not eventually eliminate the fibers concerned with certain types of pain referred to the head and deep structures of the face.

Cervicothoracic rhizotomy, including the lower three cervical posterior roots and the upper five thoracic roots, accomplishes control of the homolateral headache or vascular pain, but the resultant disability through anesthesia produced in the upper extremity does not justify this radical procedure.

The observations I have summarized indicate that pain fibers situated on the large arterial branches to the cranial structures, as well as the venous sinuses and certain tentorial ambulatory veins, follow their vascular structures, leaving the skull, face and head to descend into the upper part of the thorax by various routes and enter the spinal cord through the posterior root mechanism, between the seventh cervical and the fifth thoracic segment of the cord.

Chordotomy at the fifth cervical segment indicates that these fibers cross in a complementary way and in conformity with other pain paths and ascend in the contralateral spinothalamic tract.

The Vascular Stretch Mechanism.—Encephalography, in which there is manipulation of intracranial volume by fluid and air, indicates that "stretch" of the vascular mechanism may be produced in two ways:

1. Distention of the ventriculosubarachnoid space, producing ischemic "stretch" of the vascular structures because of the increased volume of fluid or air and thus causing headache. This headache, however, can be controlled promptly by relief of the ventriculosubarachnoid "stretch," as by the withdrawal of superfluous fluid from the venous subarachnoid spaces or an equal displacement by reduction of other volume components. Headache produced by this type of mechanism is designated as the "hydration" type and is clinically relieved by measures of dehydration, elimination, decompression, etc.

2. "Stretch" due to overfilling of the sinuses or the arterial tree, such as is produced by hyperemia associated with actual engorgement and dilatation of the veins, with compensatory displacement of fluid by another volume component. This type has been designated as the "hyperemic stretch" mechanism and is a corollary of dehydration or diminished volume in the ventriculosubarachnoid spaces or is due to the removal of some other volume component equivalent to such a displacement of fluid.

Clinical experiences with overwithdrawal of spinal fluid, overdehydration and uncompensated hyperemia (deliberately or pathologically induced) are examples of this type of mechanism. Therapeutic relief is obtained by the addition of fluid volume to the craniovertebral cavity, either by direct instillation of saline solution or by hydration by means of forcing fluids and increase in the carbohydrate metabolism by addition of greater amounts of this component to the diet, together with appropriate amounts of insulin. There is consequent gain of body weight as fluid storage is registered in the tissues, as well as in the craniovertebral cavity.

Comment.—The "hyperemic stretch" mechanism due to engorgement of the arteriovenous vascular tree and increase in cranial blood volume has been established, and this condition may follow rapid loss of the water weight of the body as well as of the craniovertebral cavity from causes which are associated with direct loss, such as spinal drainage or cerebrospinal leak, rapidly emaciating conditions or the types of the so-called neuroses associated with underweight and a tendency to diabetes insipidus.

It is obvious that a "stretch" type of hydration headache may be converted into a "hyperemic stretch" type of dehydration headache if excessive spinal fluid

is removed; the patient is not aware of the difference between the two types. The clinician is likewise not aware of the immediate shift which may have occurred in volume relationships owing to this procedure.

Headache, following spinal puncture, therefore may frequently arise when the initial "increased pressure hydration" type has been converted into a "decreased pressure and volume" type, associated with marked hyperemia. Therapeutically, the measures of dehydration should be employed for types of ischemic hydration headache demonstrable through clinical signs and objective findings; on the other hand, headache of the hyperemic type should be treated with forcing fluids, hydration of the patient and maintenance of increase in the cerebrospinal fluid reservoir.

Intracranial pathologic conditions, which claim abnormal relationships, may give rise to the "ischemic stretch" type of headache, as the cerebrospinal fluid has been interrupted in its normal circulation and overaccumulation is permitted to occur, whereas pathologic lesions that promote hyperemia (which is allowed to arise at the expense of a diminishing volume of ventriculosubarachnoid fluid) may produce the hyperemic type of "stretch" headache; either of these mechanisms, if properly compensated for by an equal shift of volume, can occur without an objective or demonstrable change in spinal fluid pressure, as registered on the manometer.

It is obvious that with the addition of 30 cc. of fluid and the subtraction of 30 cc. of blood the total volume remains unchanged; pressure relationships may remain unchanged although the physiologic behavior and symptomatology may be greatly altered; the same possibility exists in a reverse mechanism.

Summary.—A dual mechanism of headache is presented in which overstretch of the vascular components arises, owing to excessive volume or pressure contained within the cranial vasculature at a time when space for this overdistention is permitted by the appropriate yielding of some other intracranial volume component. The mechanism involves:

1. Hyperemic overengorgement of the vessels with blood within the lumen of the arteries, veins and dural sinuses (dehydration headache).

2. Abnormal stretch of the vascular tree by overdistention of the ventriculosubarachnoid fluid spaces, usually associated with increased intracranial pressure and relative ischemia.

The problems of referred vascular pain to the head have been discussed. This type of pain is not to be considered as true headache unless directly promoting or coincident with one of the two mechanisms.

DISCUSSION

DR. B. J. ALPERS: Dr. Fay has made it clear that stimulation of the pial arteries and dural sinuses produces headache in localized portions of the cranial cavity. The stimulus necessary to produce this sensory impression apparently differs in Dr. Fay's work from that in Penfield's. The latter found that stimulation of these vessels by stretching produced the sensations in question, whereas Dr. Fay produced them by electrical stimulation. It does not seem to me that this by any means explains the entire problem of headache. The mechanism is obviously much more complex. It does explain why certain types of referred pain and localized pain occur under particular experimental conditions, but it is difficult to explain on this basis the headache which one observes in cases of tumor of the brain or which one finds associated, for example, with meningitis. Can one regard this as a massive stimulation of vessels and sinuses, or is this stimulation only a small part of the mechanism involved? Dr. Fay made the further point that generalized hyperemia can produce localized headache. I wish him to explain this statement a little more, for it is difficult to comprehend how generalized hyperemia can produce headache with focal manifestations.

DR. TEMPLE FAY: I probably did not make myself clear. This is entirely a stretch mechanism. In the entire series I have encountered no patient with spot or focal localization. The subjects described headache as deep pain in a

general area, diffuse and ill defined. When one can get near the structures of the midline and stimulate the anterior cerebral arteries, the pain may be bilateral, and then there may be reference of pain to the frontal region. The best method of stimulation is stretch. This can be accomplished by picking up the arachnoid and putting stretch on the vascular tree. The headache caused by a tumor is due to a general stretch of the ventriculosubarachnoid system or to distortion and not to local irritation. This is obvious, as one can relieve this type of headache by methods of dehydration.

DR. D. J. MCCARTHY: Does Dr. Fay refer to two particular types of headache or to all types?

DR. WILLIAM L. LONG: Have there been changes in the carbohydrate content of the diet?

DR. TEMPLE FAY: In answer to Dr. McCarthy's question: one of my pupils, Miss Elizabeth Young, found 534 references to headache as a symptom in various diseases and complications of disease encountered in medicine. We have sought a common denominator through which diseases act. We can state that our studies resolve it into a dual mechanism: (1) when the ventriculosubarachnoid spaces are overdistended (toxic, hydrated type) and (2) when the vessels themselves are engorged, with overstretching of the hyperemic type. Purgation and elimination are good for the former condition, and increase of water weight, rest, retention and hydration, for the latter.

In response to Dr. Long's question about the use of carbohydrates: my associates and I have cut down carbohydrates, in order to assist in dehydrating patients, with favorable response. This is valuable in treatment of the hydrated, waterlogged type of patient. In the underweight, neurotic type we have found that carbohydrates should be increased and small doses of insulin given. This rapidly assists in water retention and refilling of the cerebrospinal fluid reservoir. This is only applying the Weir Mitchell treatment—rest and added weight.

In summary, I may say that headache arises as a symptom due to stretch of the cerebral vascular tree when extremes of hydration or dehydration are such as to alter grossly the volume relationships of the cranial cavity and bring about physical stretch on the sheath of the large arteries and venous sinuses.

MENINGEAL FIBROBLASTOMAS OF THE TUBERCULUM SELLAE. DR. FRANCIS C. GRANT and DR. ROBERT A. GROFF.

The decision that a meningeal fibroblastoma of the tuberculum sellae is present depends not alone on a knowledge of the symptoms accompanying such a lesion but on a thorough realization of the possibilities in differential diagnosis. The syndrome of tumor of the tuberculum sellae at a time when surgical removal is possible is, according to Cushing, a history of failing vision, which usually starts in one eye and subsequently involves the other, an irregular form of bitemporal hemianopia and primary atrophy of the optic nerve. The patient is usually between the ages of 30 and 50 years, corresponding to the age group for meningeal fibroblastomas.

These characteristics were found in 3 patients on whom successful operation was performed by Dr. Grant. The histories revealed loss of vision in one eye, with subsequent loss in the other. The visual fields presented an irregular form of bitemporal hemianopia. Two patients had unilateral primary atrophy of the optic nerve, with a normal fundus in the other eye. The third patient had bilateral primary atrophy of the optic nerve. The ages of the 3 patients were 51, 41 and 31 years, respectively. Roentgenograms revealed a normal pituitary fossa in 2 patients and erosion of the posterior clinoid processes and floor in the third. The tumors were small, demonstrating an early state of development, and in 1 patient complete removal was accomplished, because of the rather small basal attachment.

The condition to be considered in differential diagnosis of meningeal fibroblastoma arising from the tuberculum sellae are: parasellar lesions, primary tumors of the pituitary gland, tumors of the hypophysial stalk, pseudotumors or chronic arachnoiditis, tumors of the optic chiasm and aneurysms.

Before discussing these conditions, we may mention another alleged cause of failing vision, only to condemn its position in the items of differential diagnosis, that is, foci of infection. Too often the patient is forced to wait for possible benefits after various potential sources of infection have been removed. The delay which results makes us feel that this cause should not be considered until the aforementioned conditions have been eliminated.

The most common parasellar tumor which may offer a picture similar to that of fibroblastoma of the tuberculum sellae is meningeal fibroblastoma arising from the lesser wing of the sphenoid bone. The syndrome in cases of this tumor is that of unilateral loss of vision, which is a prominent, progressive symptom throughout the course of the disease, and involvement of the first, third and fourth cranial nerves. The visual fields show a homolateral quadrantic or homonymous contralateral defect, whereas tumors of the tuberculum sellae present a bitemporal defect. This usually serves to differentiate them. However, in spite of this auxiliary, aids may be necessary.

Primary adenomas of the pituitary gland almost always cause enlargement of the pituitary fossa before definite changes in the field can be demonstrated. This, together with signs of pituitary dysfunction, should make the differential diagnosis not difficult.

Tumors of the hypophysial stalk are generally seen in patients before the age of 25 years, whereas the meningeal fibroblastoma occurs in patients beyond this age. Furthermore, the patient with a tumor of the stalk usually presents definite signs of dysfunction and roentgenographic evidence of a suprasellar lesion. These three findings should assist in the differentiation of a tumor of the hypophysial stalk and a fibroblastoma of the tuberculum sellae.

Pseudotumor or chronic localized arachnoiditis occurs more frequently in the posterior fossa than around the pituitary fossa; according to Frazier, the symptoms of increased intracranial pressure precede the localizing symptoms, sometimes by years. Frazier is in agreement with Donner that the duration of the illness in this condition is much longer than that in intracranial neoplasm. These facts help in the diagnosis of so-called pseudotumors; yet there are instances in which it is extremely difficult to distinguish pseudotumor from a suprasellar tumor, when it occurs in the region of the pituitary fossa.

Gliomas of the optic chiasm and aneurysms are rare; the former are seen chiefly in childhood or early adult life. Aneurysms usually present localized erosion and may be associated with positive serologic reactions for syphilis.

The diagnosis of a tumor of the tuberculum sellae is not difficult when the aforementioned conditions and their characteristics are kept in mind. The approach to the diagnosis should be the elimination of each possibility before the consideration of toxic or intrinsic disease of the eye. When such a plan is followed, meningeal fibroblastomas of the tuberculum sellae and other lesions in this region will be recognized when surgical intervention can offer the return of normal visual function.

DISCUSSION

DR. TEMPLE FAY: This is an interesting analysis, and the authors are to be congratulated. One possible explanation of the time required for visual symptoms to develop, which Dr. Groff pointed out, is, I believe, the anatomic type of chiasm which is present. Dr. de Schweinitz, in his Bowman lecture, called attention to the three types of anatomic relationships of the chiasm. Dr. Schaeffer worked out the anatomic relations when the optic nerves are long. One may find the prechiasmal syndrome, with pressure on one or both nerves giving bizarre field cuts. In the short chiasmal type one may observe a retrochiasmal syndrome, with pressure on the optic tracts and, hence, homonymous hemianopia in the normal chiasmal group bitemporal hemianopia is to be expected.

DR. ROBERT A. GROFF: At the operating table we were unable to tell whether or not the chiasm was fixed. The type of chiasm seems to offer a reasonable explanation why some patients waited for one year and others much longer.

Book Reviews

Human Mentality in the Light of Psychiatric Experience: An Outline of General Psychiatry. By Bror Gadelius. Cloth, 33 Danish crowns; 30 shillings. Pp. 620, with 49 illustrations. Copenhagen, Denmark: Levin and Munksgaard; London: Oxford University Press, 1933.

Gadelius, professor emeritus of psychiatry at the Karolinska Institute of Stockholm, Sweden, gives to English-speaking colleagues the first volume of a translation of this fruit of his life-work. It is in itself a well rounded outgrowth of a scholarly and, at the same time, a practical career as teacher and head of an institution; it is true to the substantial and conscientious traditions of the formal psychology of Scandinavian schools and yet in the end arrives at a genuinely human preparation for medical studies. Gadelius develops an empirical psychology, with a remarkable result, surprisingly similar to what happened in the development of psychology in America, although he is perhaps more careful to work in the essentials of the conservative picture of the teachings of the years of transition. "Psychiatry is not only psychology; rather, its attitude is psychobiological"; it is a branch of medicine. It is against the background of the normal life that mental diseases are studied; if the "natural sciences" fail to keep themselves open to matters as found in life, it becomes necessary to expand them or to add what is needed to do justice to actual experience.

For any one interested in the transition from the psychiatry of the nineteenth century to that of the twentieth, the present work is an excellent representative, if not the best, to the knowledge of the reviewer.

It begins with a sketch of the history of psychiatry, with many data from the northern countries not widely known and, at the same time, an intimate knowledge of other European developments not often adequately reviewed. Epistemology begins to yield to genetic-dynamic considerations, with liberalization of the rigid German concepts, through the more comprehensive cultivation of a wider range of workers and points of view. Freud's work is given a critical discussion in the third part of the book, devoted to treatment. "Few methods are so exposed to further bungling by laymen as psychoanalysis." To a man with as broad a foundation as that of Gadelius, no gospel of exclusive salvation will be suitable. In spite of the somewhat formal chapter headings of the section on the functional structure of mental life and its morbid changes (pages 84 to 368) and of the second section, on the causes of mental diseases (pages 369 to 524), there is such a wide knowledge of the literature and such sound reference to actual experience that the reader cannot but admire what the author has brought before his Swedish students.

Thus, the title "Human Mentality in the Light of Psychiatric Experience" is thoroughly becoming to the work. Its appearance in English is fortunate. Our investigators will profit from the reading of this substantial contribution and the orientation it gives.

Psychopathology: A Survey of Modern Approaches. By J. Ernest Nicole, with Foreword by W. H. B. Stoddart. Second edition. Cloth, $4.75. Pp. 283. Baltimore, William Wood & Company, 1934.

The author offers an orientation in modern psychopathology in its broadest sense, including the leading theories and investigations and the treatment based on them. The only field omitted is histopathology. An enumeration of the headings of the various chapters will perhaps convey the best idea of the scope of the book: historical survey; Morton Prince; Freud's psychoanalysis; Adler's individual psychology; Jung's analytic psychology; Rivers' theories; Watson's behaviorism; Kempf's psychopathology; Berman's endocrine theories; biochemical and physiology contributions; Kretschmer's constitutional approach; ethnologic and sociologic evidence; the eclectics and the characterologists; the position in psychology; applied psychopathology; the concept of the ego in psychiatry; type psychology, with special reference to Jung, and psychopathology and the herd instinct. The carefully selected bibliography, with an index of names and authors, is a valuable help.

The presentation is concise and interspersed with critical remarks and references. This, however, does not make for easy reading, and one frequently wishes that the author had given more consideration to some of the fundamental theories and approaches. The theories of Kretschmer and Jung concerning constitutional types hardly deserve so much space in this condensed presentation, and a fuller discussion of the group of eclectics would have been more welcome. One might also wonder whether Prince, Rivers, Kempf and Berman are not given too important a position.

The book is valuable for the wealth of material presented. This wealth, however, confirms the opinion that modern psychopathology is more interested in presenting stimulating theories than in a careful and critical study of facts.

Zur Psychopathologie und Klinik der Angstzustände. Sonderausg. von Abhandlungen aus die Neurologie, Psychiatrie, Psychologie und ihren Grenzgebieten. By Dr. Gustav E. Störring. Pp. 117. Price, 7.80 marks. Berlin: S. Karger, 1934.

In the introduction the author discusses the main theories of anxiety according to older authors (Darwin and Ribot) and also Freud and Goldstein. He includes fear and offers three types: anxiety with recognition of danger to oneself or persons close to oneself, anxiety due to objective danger without recognition and toxic and reflex anxiety. After a discussion of various degrees of intensity, he discusses pathologic anxiety. The first part deals with "pure" anxiety states, a term which is defined rather vaguely, with reference to various types and degrees of anxiety and their somatic and emotional aspects. The second part refers to anxiety in various psychopathologic settings. The author presents the relationship of anxiety to perplexity, to depressive and paranoic reactions and to compulsions. Perplexity and anxiety are two different emotional reactions, although always closely connected. In depressions anxiety is always present, even though expressed only as inner restlessness. Suspiciousness is derived from anxiety. In paranoic reactions the emotion of irritability is coupled with anxiety. Compulsive acts are accompanied by anxiety, which results from the fundamental contrast of strong emotions and weak volitional tendencies in the constitutional make-up of these patients. Hypochondriasis is anxiety about oneself and anxious self-observation.

This purely phenomenologic descriptive study is not wholly satisfying, although it is interesting as the expression of one of the leading German psychiatric schools.

Die Ursprünge des Verbrechens. Dargestellt am Lebenslauf von Zwillingen. By Dr. Friedrich Stumpfl. Boards, 5.80 marks. Pp. 176, no illustrations, 3 plates. Leipzig: Georg Thieme, 1936.

This book is based on a study of sixty-five pairs of twins who showed criminal behavior. Of fifteen pairs of identical male twins, there was similarity of criminal behavior in nine pairs and dissimilarity in six pairs. Of seventeen pairs of fraternal male twins, seven exhibited concordance and ten discordance of criminal behavior; of three pairs of identical female twins there was concordance in two pairs and discordance in one pair, and of two pairs of fraternal female twins, there was dissimilarity of criminal behavior in both pairs. Résumés of the records of all the pairs of the same sex comprise roughly two fifths of the book. All the identical twins are reported to have been similar in every-day social adjustment, character structure and the configuration of psychopathic tendencies, while the fraternal twins were always different in these respects.

The author concludes that some criminality is of hereditary origin and should lead to sterilization. He appears to neglect adequate attention to the effects, pointed out by von Bracken, of the high degree of mutual intimacy and identification typical of identical twins and the lesser degree of intimacy and the tendency to rivalry common to fraternal twins as influences promoting the resemblance in personality of identical twins who are reared together, as compared with that of fraternal twins. This influence doubtless results in a resemblance in behavior of identical twins, in addition to that due to heredity alone. This resemblance would be ascribed to heredity by Stumpfl.